MIT Technology Review

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35 INNOVATORS UNDER 35
p50

Code that reduces bias in hiring—and 34 other ideas that will shape the future.

Meet Stephanie Lampkin and the rest of the 2016 Innovators Under 35 inside.

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From the Editor

GUIDO VITTI

Seven over 70

Our annual list of 35 innovators under the age of 35 inevitably arouses this objection: "Do you really believe older people aren't innovative?" Of course they are. We write about the young because we want to introduce you to promising researchers and entrepreneurs. But older people are as capable of new thinking as young ones. Below are seven innovators over the age of 70, still working.

1. **Shirley Ann Jackson**, 70, is the 18th president of Rensselaer Polytechnic Institute. A theoretical physicist, she was the first African-American woman to be awarded a doctorate from MIT, and she is widely admired for making Rensselaer into a major center of research. She has served on a bewildering number of public committees, including President Obama's Intelligence Advisory Board, where she is cochair, and the Nuclear Regulatory Commission, which she chaired from 1995 to 1999.

2. Research conducted and startups founded by the computer scientist **Michael Stonebraker**, who is 71, led directly to the relational databases used everywhere today. He worked for many years at UC Berkeley and in Silicon Valley; and as an adjunct professor at MIT and an entrepreneur, he continues to cofound a new company every couple of years, commercializing his breakthroughs in database management. In 2014, he received the Turing Award.

3. The philosopher **Derek Parfit**, born in 1942, published *Reasons and Persons* in 1984 to immense acclaim. Using thought experiments borrowed from science fiction, including speculations about teleportation, the book exploded ideas about the persistence of identity and our duties to future generations. There followed a 37-year near silence, while a monumental unfinished work was circulated in manuscript amongst philosophers and reading groups. In 2011, Parfit finally published *On What Matters*. It reconciles rules-based, consequentialist, and contractualist conceptions of morality, which Parfit says are "climbing the same mountain on different sides."

4. **Matthew Carter**, 78, is one of the most prolific type designers in history. More than anyone else, Carter is responsible for translating classic type to digital uses. His fonts include Georgia, designed to be legible even on very small or low-resolution screens and included in the "core fonts for the Web" bundled with Internet Explorer 4.0. His greatest typefaces, including Miller, Verdana, and Walker, are displayed in the permanent collection of MOMA.

5. **Donald Knuth**, also 78, is a professor emeritus at Stanford University and the author of the influential multivolume *The Art of Computer Programming*. It was initially conceived as a single book of 12 chapters in 1962, but Knuth retired from teaching in 1990 in order to complete the series, whose Volume 4, Fascicle 6 (on "Satisfiability"), was released in December of last year.

6. The environmental microbiologist **Rita Colwell**, born in 1934, was the director of the National Science Foundation from 1998 to 2004 and is now a professor at the University of Maryland and Johns Hopkins University, chairman emeritus of Canon U.S. Life Sciences, and CEO of CosmosID, a genomics company using data analysis to identify microörganisms for diagnostics, public health, and drug discovery. In 2006, Colwell was awarded the National Medal of Science.

7. **Ruzena Bajcsy** is a roboticist who is still actively publishing at the age of 83. Born and educated in Czechoslovakia (where the Nazis killed most of her relatives, orphaning her at 11), she was a professor of electrical engineering at the University of Pennsylvania, led the Computer and Information Science and Engineering Directorate of the National Science Foundation with its $500 million budget, and is today a professor at UC Berkeley, where she is also director emerita of the Center for Information Technology Research in the Interest of Society. Her current research focuses on AI, computational biology, and biosystems. Last year, she cowrote three papers about using Microsoft Kinect to improve the lives of older adults or people with muscular dystrophy.

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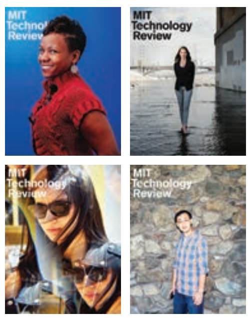

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Letters and Comments

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Volume 119, Number 4

Why Universal Income Is No Sellout

David H. Freedman, in his July/August article provocatively entitled "Basic Income: A Sellout of the American Dream," erroneously dismisses the idea of a universal basic income, citing his analysis and those of a series of "experts."

Freedman's rejection of a universal basic income is built on two highly debatable points: 1) that large-scale technological unemployment isn't happening and won't anytime soon; and 2) that existing safety-net programs could be expanded to eliminate poverty. The amount of reputable research grows every day as to the possibility of technologically driven unemployment. The McKinsey Global Institute's research finds that today's technology could eliminate 45 percent of all present tasks, with artificial intelligence reducing 13 percent more; the Boston Consulting Group estimates up to 25 percent job loss in the U.K. by 2025.

A 2014 Pew study of 1,896 experts produced these results: "half of these experts (48 percent) envision a future in which robots and digital agents have displaced significant numbers of both blue- and white-collar workers—with many expressing concern that this will lead to vast increases in income inequality, masses of people who are effectively unemployable, and breakdowns in the social order."

A new report by Citigroup forecasts that retail banking automation could eliminate nearly two million jobs. As driverless trucks get ready for the highway, what happens to the 3.5 million truck drivers—the most common job in 29 states—and the 5.4 million workers in auto repair, insurance, sales, and rest stops?

Rather than dismiss a universal basic income, we should embrace the concept and do experiments to compare it with other solutions, such as guaranteed jobs.

A universal basic income can help do now what our welfare system completely fails to do: end poverty. It can be well researched, vetted, and ready to go before massive disruption threatens our social order and inflicts more economic pain.

My proposal of $1,000 a month for adults aged 18 to 64 creates a floor that enables every American to live above the federal poverty line. It supplements work and provides lower-income families with the stability and ability to take risks that middle-class and wealthy parents have. That stability to cosign for a child's apartment or help pay for car repairs and medical bills is an extraordinary gift.

Freedman is right about deploying short-term measures now, but as a long-term prescription his ideas are the real sellout for those who will be underwater during the transition, and for the accountants, truck drivers, and retail workers whose jobs will be washed away.

—**Andy Stern, author of *Raising the Floor: How a Universal Basic Income Can Renew the Economy and Rebuild the American Dream***

Freedman's ideas are the real sellout for the truck drivers and retail workers whose jobs will be washed away.

David Freedman responds:

There's little evidence that technology is leading to a net loss of jobs or that such an effect is imminent. Mr. Stern misquotes the BCG study, which predicts that the percentage of automatable tasks that are actually automated will rise from 10 percent today to 25 percent in 2025—not remotely the same as a 25 percent job loss by 2025. Yes, more jobs are being lost to automation, but new ones are being created. The pain we see around us is due to the fact that the new jobs require more skills than most Americans have, or different ones. Handing everyone in the country $1,000 a month is an expensive and, for the jobless, potentially demeaning way to solve that problem. Better to reëngage people in the economy through education, training, job creation, and incentives.

Correction

In "The All-American iPhone" (July/August), hafnium was erroneously described as a rare earth metal.

Twitter Votes

Reactions to our stories on the iPhone, Oculus Rift, universal basic income, and Hyperloop.

If the iPhone were made in America, it would be more expensive. How much more would you be willing to pay?

54%	Nothing
28%	\$10–\$100
18%	\$100–\$200

What are you most looking forward to doing in virtual reality?

48%	Playing games
33%	Watching films
19%	Hanging out with friends

A “universal basic income” would give all citizens a cash payout to combat tech-related unemployment. Would it work?

41%	No; we shouldn’t be idle
34%	Yes; the 1% owe us
25%	Depends on the payout size

Which pet project from tech billionaires do you think would most improve the world?

42%	Hyperloop
33%	Extending human life spans
25%	Mars colonies

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Views

Y-Vonne Hutchinson

Allison Macfarlane

Olga Russakovsky

ANDY FRIEDMAN

INNOVATION

Biased by Design

Exclusion hurts tech companies more than they know.

A few months ago, my boyfriend convinced me to use Snapchat. He was taking goofy pictures and wanted me to join him. But when I tried, the app would map my face, and—nothing. We changed positions. We tried improving the lighting. Nothing worked. I started to get that familiar sinking feeling in my stomach, the flush of heat to my face. Growing up in Texas, I received many negative messages about my dark skin. Now here I was, 20 years later, too black for Snapchat.

Today, we recognize that the tech industry has a problem with bias—conscious and unconscious. The business case for diversity has been established—in 2015, McKinsey found that diverse teams perform better over the long term (see Innovator Under 35 Stephanie Lampkin, page 69). But we're also finding the immediate benefits of diversity. Businesses need people who can identify a company's blind spots—and the more homogenous the team, the bigger the blind spot.

Companies that lack diversity risk building products that exclude their customers—my experience with Snapchat being one example. Sometimes the exclusion is more blatant, as when Amazon was discovered in April to be excluding black neighborhoods from its next-day delivery service.

Exclusion isn't the only way disenfranchised groups feel pushed out. Facebook has come under fire for suppressing posts supporting Black Lives Matter or conservative politics. People who send death threats via networks like Twitter often face only delayed or underwhelming repercussions.

Biases can become embedded in a product during any period of the development process. If the people making the products happen to come from a group that rarely experiences discrimination, those people will have a harder time predicting how bias will manifest itself. As an example, a recent study found that Airbnb guests with African-American names were 16 percent less likely to find lodging. Airbnb itself may have been shocked by that, if only because most Airbnb employees don't encounter that kind of bias in their own lives.

Unconscious biases woven into the DNA of a firm can be passed down from team to product to user. And these blind spots have consequences. They can lead to low levels of adoption, premature market saturation, and broken products.

Simply put, diversity increases the likelihood of a tech company's survival. Nearly half of all new businesses survive their first five years, but only 10 percent of tech startups survive past the first 18 months. An estimated 42 percent of tech-startup failures can be attributed in part to a fundamental misunderstanding of the market. A company with a diverse team that's capable of recognizing gaps in organizational thinking is less likely to have a crippling blind spot than one with a homogenous team. An organization that sees, understands, and is able to respond to its market is more likely to thrive than one that can't.

Y-Vonne Hutchinson is the founder of ReadySet and a founding member of the advocacy group Project Include.

ENERGY

Nuclear's Glacial Pace

There's a reason it takes so long to approve a new reactor design.

Climate change has forced us to rethink how we get electricity. Use of renewable sources like solar and wind is rapidly

increasing, while nuclear, though long a reliable source of carbon-free electricity, is not. Meanwhile, a number of startups are promising cheap, safe, proliferation-resistant nuclear energy in the next decade (see "Fail-Safe Nuclear Power," page 38).

Can these startups fulfill their promises? Outside of China, nuclear power is expanding nowhere. China has 21 new reactors under construction; Russia has nine, India six. The U.S. is bringing five new plants online, but since 2012, five other reactors have been retired, with seven more to be shuttered by 2019. California's Diablo Canyon plant recently announced it will close by 2025. With other plants closing in Japan, Germany, and the U.K., more reactors may be decommissioned than built in the near future.

So why is this happening? Because it's expensive and time-consuming to design and build a new nuclear plant, and there are cheaper, easier alternatives.

The U.S. Nuclear Regulatory Commission has been waiting since 2014 for applications for design certification licenses for small modular reactors—smaller versions of the large and extra-large operating light-water reactors, with additional safety features. Such plants, which could be factory-built and snapped together on site, hold the promise of providing cheaper nuclear power in a more distributed fashion. Other designs are on the horizon, including molten-salt reactors, which are promising but won't be ready for decades.

In 2015, the General Accountability Office reported that it takes 20 to 25 years to develop a new reactor in the United States—10 years for the design phase, 3.5 years for a design certification license from the NRC, four years for a combined operating license, and another four years for construction. And that's only in an ideal world where no unexpected problems occur.

The GAO also found that it's not cheap to bring a design to fruition: just to reach the design certification point costs somewhere between \$1 billion and \$2 billion, and only about \$75 million of that is NRC fees. There's a reason it takes so long and costs so much: manufacturers need to confirm that the design is safe and secure.

Some people blame the regulators for holding up the plants. Yet the NRC hasn't been presented with any applications for new reactors and probably won't be for years. Data from prototype plants would be helpful, but then many of the "new" designs are not so new at all. Sodium-cooled fast reactors have been built by countries including the U.S., Japan, Russia, Germany, France, and India since the 1950s, but no country has been able to make a plant cheap and reliable enough to even come close to being a viable energy source.

Yes, new nuclear technology can provide carbon-free electricity. But it has to do more than that. It has to be safe, secure, and resistant to proliferation. It has to compete in the marketplace. New nuclear designs are promising, but they're no short-term solution to the climate problem.

Allison Macfarlane was the chairman of the Nuclear Regulatory Commission from 2012 to 2014.

COMPUTING

AI's Research Rut

When we think of AI as one particular thing, we drag the whole field down.

When you picture AI, what do you see? A humanoid robot? When you think about a real-world application of AI, what comes to mind? Probably autonomous driving. When you think about the technical details of AI, what approach do you name? I'm willing to bet it's deep learning.

In reality AI comes in many shapes and forms. AI machines go far beyond humanoid robots; they range from software detecting bullying on social media to wearable devices monitoring personal health risk factors to robotic arms learning to feed paralyzed people to autonomous robots exploring other planets. The potential applications of AI are limitless: personalized education, elderly assistance, wildlife behavior analysis, medical-record mining, and much more.

Our failure to appreciate this spectrum threatens to hold back the field. When we collectively picture AI as one type of thing—whether it's humanoid robots or self-driving cars or deep learning—we're encouraging the next generation of researchers to be excited exclusively about those narrow things. If students are presented with a homogeneous pool of AI research role models, then it's a self-fulfilling prophecy that only students who "fit in" will remain in the field.

Since AI has enticingly broad possible applications, we need people with a comparably broad set of experiences and worldviews working on AI problems. Wouldn't research teams working on AI medical applications benefit from researchers trained in biology? Wouldn't teams working on AI hunger relief benefit from researchers with firsthand experience in poor countries? Wouldn't teams working on AI assistive devices benefit from researchers with physical disabilities?

Today there's a lot of fascinating work going on in AI (see "AI's Unspoken Problem," page 28), but we're also kind of in a rut. We've tended to breed the same style of researchers over and over again—people who come from similar backgrounds, have similar interests, read the same books as kids, learn from the same thought leaders, and ultimately do the same kinds of research. Given that AI is such an all-encompassing field, and a giant part of our future, we can't afford to do that anymore.

Olga Russakovsky is a postdoctoral research fellow at the Robotics Institute of Carnegie Mellon University.

Upfront

SARAH MAZZETTI

Gene Therapy Is Curing Hemophilia

Spark Therapeutics is turning decades of experiments into real drugs.

Earlier this year, Bill Maurits sat in a waiting room in Philadelphia ready to have a trillion viruses dripped into his body through an IV. Maurits has hemophilia B, which means his body doesn't produce enough factor IX, a protein that clots blood. He's at risk for bleeding, and his joints are damaged from all the bruises. Since he was 10,

Upfront

he's depended on injections of "ridiculously expensive" replacement protein.

In April Maurits, an engineering designer, joined a study in which he was dosed with viruses packed with a correct version of the gene that codes for factor IX. The Philadelphia company that ran the gene-therapy study, Spark Therapeutics, reported that in all four patients, factor IX activity has reached about 30 percent of average. That's enough to prevent bleeding when you get hit by a baseball or twist your ankle. It's also been enough to let Maurits go without factor IX replacements since April. "There's no other explanation than 'It worked,'" he says.

Sure, gene therapy has been tried before. What's different is that Spark's therapy so far appears to work well every time it's attempted—a consistency that's eluded previous efforts. "Right now this looks very close to being as good as it gets," says Edward Tuddenham, a hematologist at University College London, who led a competing study and consults with some of Spark's rivals.

The results are satisfying news for people like Maurits, as well as for scientists who've struggled for three decades to get gene therapy right. Two gene therapies for ultra-rare inherited disease are approved in Europe, including one to treat severe immune deficiency.

But hemophilia could be the big one. It affects about one in 5,000 men (women are rarely affected), and there's a $10-billion-a-year market in blood factor replacements. Only a larger study will determine whether Spark's treatment works. "This is four subjects. We are going to need more," says Katherine High, the hematologist who is Spark's president and founder. "If you saw that in 40 subjects, then maybe ... well, it's very exciting."

"For gene therapy, hemophilia isn't the finish line. It's just the start."

Spark does have competition. Gene therapy is booming, with about 70 products in late-stage testing. UniQure and Baxalta are both testing gene therapies for hemophilia B. And the drug company BioMarin is testing a genetic fix for hemophilia A, the more common type; it has reported results in eight patients, and Tuddenham calls them just as impressive as Spark's.

Some scientists say it's too soon to declare success, since patients' factor levels are still short of normal. "I wouldn't say they've found the cure, but this is the first time it looks good," says Federico Mingozzi, a gene-therapy scientist at France's INSERM research institute. "The true innovation is that they have really had a consistent result. I haven't seen that before."

If gene therapy succeeds, hold on tight. One-time cures for devastating illnesses could command eye-popping prices of $1 million a dose, perhaps more. But it might be worth it and then some, says Mark Skinner, a lawyer and former president of the World Federation of Hemophilia. He says treating his severe case of hemophilia already requires $750,000 worth of drugs.

The road to Spark's therapy began in 1989 when High, then a professor, helped isolate the canine version of factor IX. Within a decade, she says, gene therapy was consistently curing dogs—more than 100 so far. Attempts to treat people ran into trouble, however. In 2006, High showed that gene therapy increased factor IX in human patients. But the effect was undone by an immune reaction never seen in dogs. The patients' corrected cells got attacked, and the effects, at first promising, wore off.

Spark was formed in 2013, when High spun her gene-therapy research group out of Children's Hospital of Philadelphia. She says Spark needed to find a way to administer viruses in a dose too low to trigger the immune system, yet large enough to get factor IX levels up. It started by redesigning a virus to take

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TO MARKET

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Plume is betting that the challenge of running a home wireless network good enough for ultra-high-definition television, video games, and the Internet of things means consumers are ready to pay extra for high-quality managed Wi-Fi. The company offers a different take on the Wi-Fi router. It sells highly designed, palm-sized routers that plug into outlets around your home; they're controlled via a cloud-based brain that's actively managing how your home network functions. Connect one into your modem, download an app to create your network, and then plug the rest into their respective rooms, where they find the network using Wi-Fi. —*Stacey Higginbotham*

DNA straight to the liver, where factor IX is made. An unusual case in Italy provided another boost. A healthy young man turned up with a serious blood clot in his leg; he turned out to have a variant of factor IX that was hyperactive, causing 776 percent of normal clotting. Bad for him. But brilliant serendipity for High's team, which seized on the hyperactive gene, called the Padua variant, as a way to produce stronger effects. At Spark's lab, High points down a gleaming white hallway lined with clean rooms where the viral particles are made. Spark can insert genes into them. Infused into a patient, they rush to liver cells and deposit the new DNA.

One measure of how well things are going: High says the FDA is concerned patients might produce *too much* factor IX. That would mean they'd have the same problem as the Padua man. "The regulatory agencies don't want you to go above 100 percent," she says. After a decade of attempting to get any effect at all, she says, "it's amazing to think you could do too well."

One huge asterisk remains: about 40 percent of hemophiliacs can't be helped yet, because the type of virus used in this therapy is similar to one that naturally infects people. The result: many people have virus-grabbing antibodies in their blood that would intercept Spark's treatment. Such patients have been excluded from the study. High is working on ideas to overcome the problem, including releasing decoy viruses to soak up the antibodies. Xavier Anguela, a Spark scientist, says if they beat hemophilia they'll quickly start working on many other rare diseases that can also be treated by adding genes to the liver—for instance, rare enzyme deficiencies like Fabry's disease. "For gene therapy, hemophilia isn't the finish line," he says. "It's just the start." *—Antonio Regalado*

ERIC PIERMONT/AFP/GETTY; COURTESY OF GM; COURTESY OF NISSAN

REVIEW

The Driverless Road Ahead

To glimpse the future of driving, take these systems for a spin. By Will Knight

Tesla Autopilot

Part of a $2,500 package, Tesla's semi-autonomous driving software launched last year via a wireless update to cars with the necessary hardware. Forward-facing radar and cameras, along with 12 ultrasonic sensors, monitor the road around the car, and Autopilot can keep within the lane, or change lanes at the tap of the turn signal. Tesla asks drivers to keep their hands on the steering wheel at all times, which is especially important following a fatal crash involving Autopilot earlier this year.

GM Super Cruise

A similar system will be offered on the Cadillac CT6 in 2017. Super Cruise will rely on similar sensors to Autopilot's, and GM has said the system will be able to drive "hands free" in a range of different situations, including bumper-to-bumper traffic and highway driving. Before long, other GM vehicles will be equipped with similar technology. The automaker acquired an automated driving startup called Cruise this year for $1 billion, and invested a similar amount in the taxi company Lyft.

Nissan ProPILOT

A more basic semi-autonomous system will be available on Nissan's Serena minivan in Japan this year, followed by models in the U.S., Europe, and China. ProPILOT relies on a single camera to track lane markings and the vehicle ahead, and it requires more driver supervision than Autopilot. It will issue warnings if a driver takes his hands off the wheel, and will disengage if those warnings are ignored. And if the car comes to a stop, the driver will need to reactivate the system.

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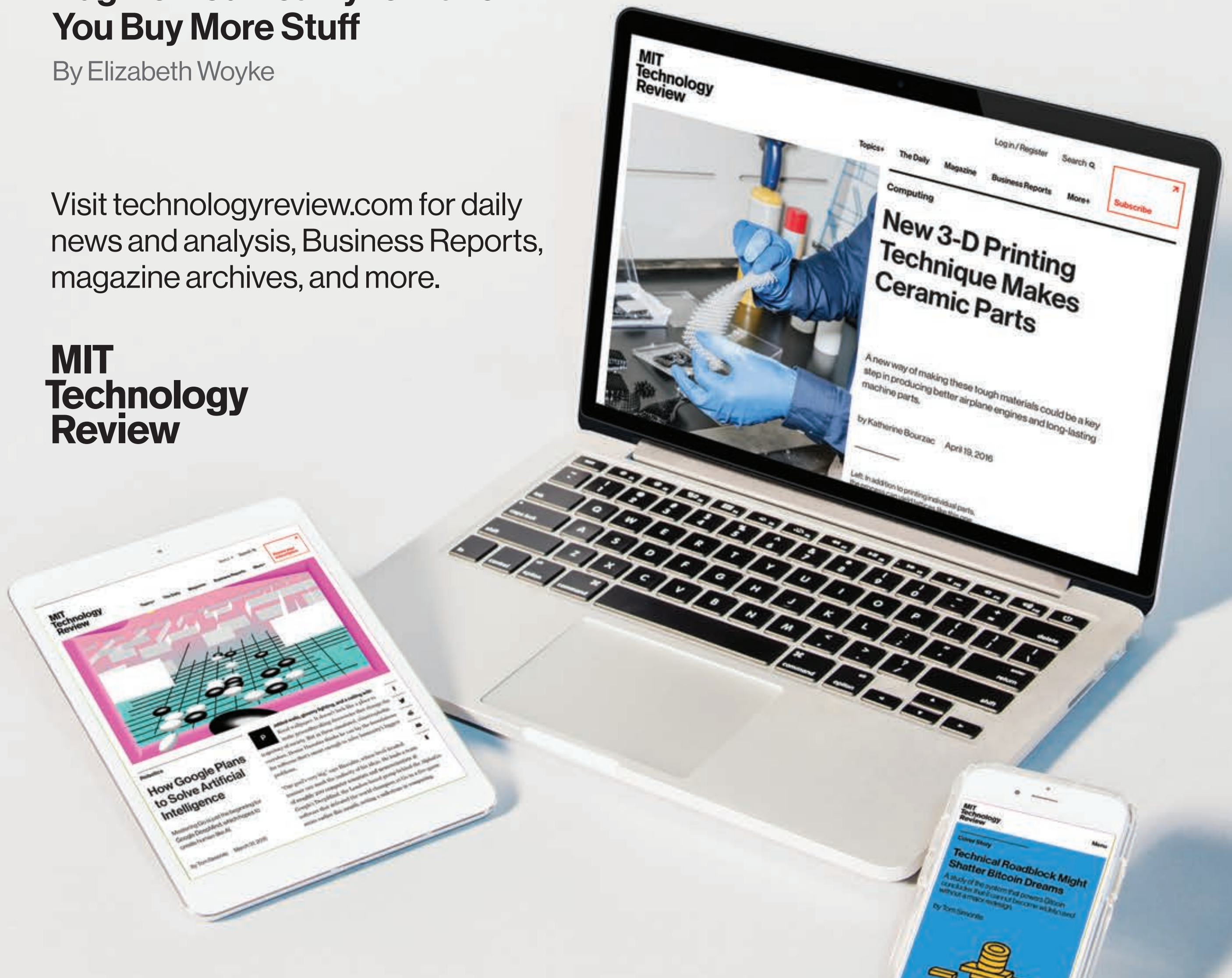
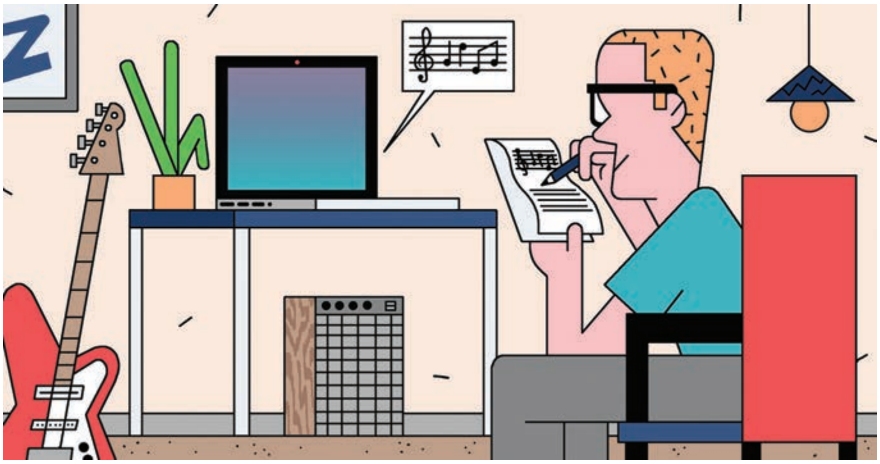


Computer, Write Me a Song

Google says its AI software could make creative suggestions to help musicians, architects, and visual artists.



ANDREA CHRONOPOULOS

Last summer the Internet was overrun by psychedelic images: swirling skies sprouting dog faces, Van Gogh masterpieces embellished with dozens of staring eyes. By running their image-recognition algorithms in reverse, Google researchers had found they could generate images that some call art. At an auction in February, a print made using their "DeepDream" software fetched $8,000.

But DeepDream images are limited, says Douglas Eck, a researcher in Google's main artificial-intelligence research group, Google Brain. Now a new Google project called Magenta is aimed at making creative software that can generate more sophisticated artworks using music, video, and text.

Magenta will draw on Google's latest research into artificial neural networks, which underpin what CEO Sundar Pichai calls his company's "AI first" strategy. Eck says he wants to help artists, creative professionals, and just about anyone else experiment and even collaborate with creative software capable of generating ideas.

"As a writer you could be getting from a computer a handful of partially written ideas that you can then run with," says Eck. "Or you're an architect and the computer generates a few directions for a project you didn't think of."

Those scenarios are a ways off. But Project Magenta collaborator Adam Roberts has demonstrated prototype software that gives a hint of how a musician might collaborate with a creative machine. He tapped out a handful of notes on a virtual Moog synthesizer. At the click of a mouse, the software extrapolated them into a short tune, complete with key changes and recurrent phrases. The software learned to do that by analyzing a database of nearly 4,500 pop-music tunes.

Can a machine ever be an artist in its own right, not just a tool directed by a human?

Eck thinks it learned how to make key changes and melodic loops because it uses a crude form of attention, loosely inspired by human cognition, to extract useful information from tunes it has analyzed. Researchers at Google and elsewhere are using such attention mechanisms to make learning software capable of understanding complex sentences or images (see "AI's Unspoken Problem," page 28).

Ideas that helped Google's AlphaGo software beat one of the world's top Go players this year could also help the quest for creative software. AlphaGo's design made use of an approach called reinforcement learning, in which software picks up new skills a little like an animal—it is programmed to try to maximize a virtual reward. Eck thinks reinforcement learning could make software capable of more complex artworks. For example, the sample tunes from Magenta's current demo lack the kind of larger structure we expect in a song.

Google's project could bring more attention and resources to a field of research that has existed for a long time in academia but is smaller than areas of artificial intelligence with more obvious business applications, says Mark Riedl, an associate professor at Georgia Tech, who creates software that creates stories and video games. However, he notes that Google's move into creative artificial intelligence is unlikely to yield quick progress on a question that looms over the field of computational creativity: can a machine ever be an artist in its own right, not just a tool directed by a human artist?

Good human artists generally start out emulating established artists before developing new styles and genres of their own, guided by an evolving artistic motivation, says Riedl. How software could develop artistic autonomy is unclear. "Neural networks are kind of in the imitation mode," he says. "You can pipe in the works of the classics and they'll learn patterns, but they need to learn creative intent somewhere." *—Tom Simonite*

Upfront

Tech Giants Go to Washington

As they try to gain more influence with regulators and policymakers, several of the top technology companies are increasing the amount of money they spend on lobbying. Some issues, like copyright policy and tax law, are of common concern. Others—like Amazon's focus on aviation (read: delivery drones)—reflect unique priorities.

TOP ISSUES 2015

Apple	Alphabet	Amazon	Facebook	Microsoft
Taxes	Intellectual property	Computers and IT	Immigration	Taxes
Intellectual property	Labor, antitrust and workplace	Taxes	Computers and IT	Immigration
Telecommunications	Consumer product safety	Consumer product safety	Intellectual property	Telecommunications
Computers and IT	Homeland security	Aviation and airports	Homeland security	Computers and IT
Trade	Telecommunications	Transportation	Taxes	Intellectual property

Overall Top Spenders

Google's parent isn't in the top 10, but it spent more on lobbying last year than longtime D.C. players such as AT&T and Lockheed Martin.

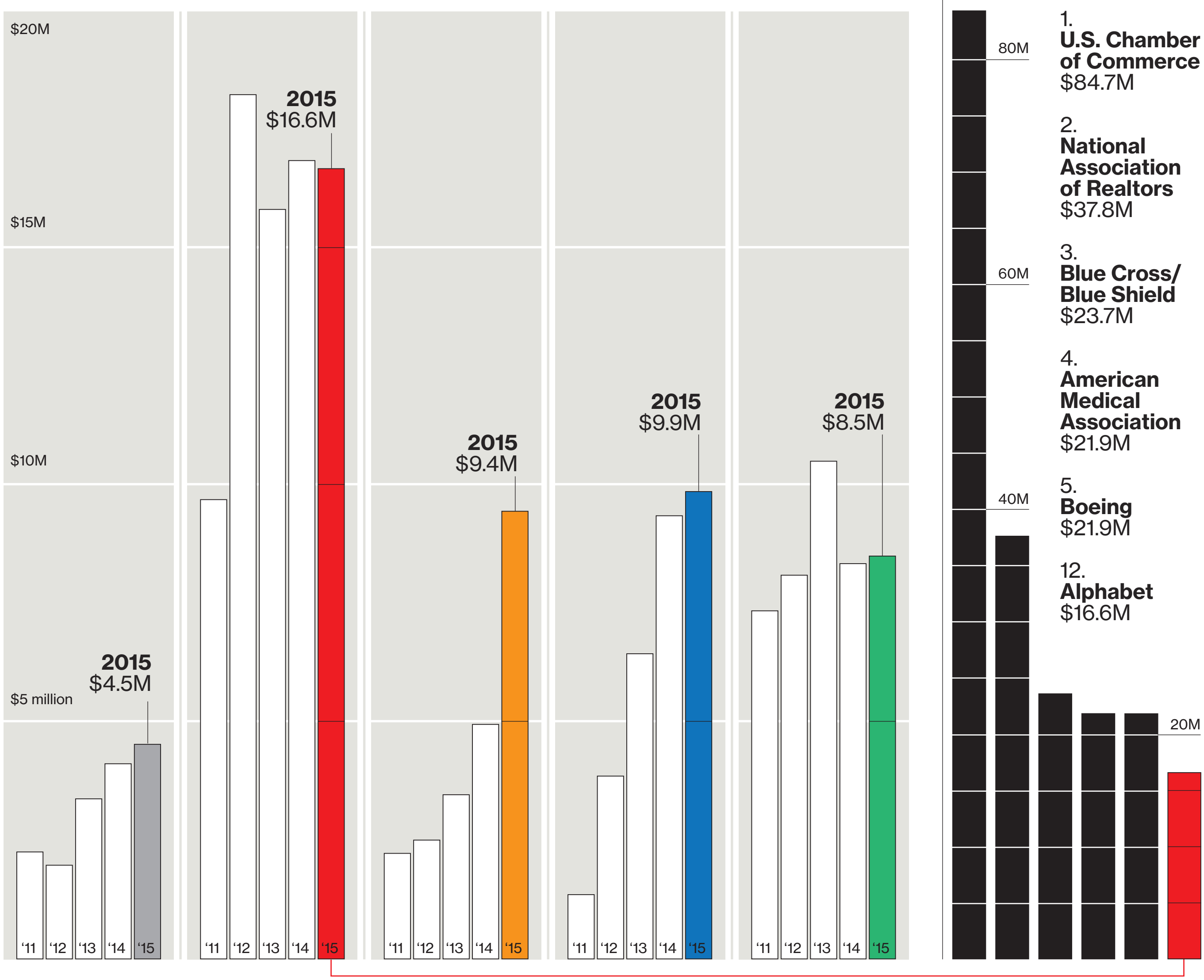


ILLUSTRATION BY LUKE SHUMAN; DATA FROM THE CENTER FOR RESPONSIVE POLITICS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Upfront

The Elusive Solar Fuel

We can now efficiently split water to make hydrogen, but a practical way to make fuels via artificial photosynthesis remains a distant goal.

When I visited Lawrence Berkeley National Laboratory this spring, Frances Houle, the deputy director of the Joint Center for Artificial Photosynthesis, showed off one of the center's latest advances. It is a device that breaks down water into hydrogen and oxygen in sunlight. Researchers had previously used artificial light to drive the process; this was the first time they were doing it with natural light. Fixed to a thin metal stand on the roof, the small device has a solar cell that supplies the energy needed for a chemical catalyst to split the water. At the top of the device, pure hydrogen bubbled up.

Created in 2010 under Secretary of Energy Steven Chu, the center, commonly called JCAP, has an audacious goal: to create fuels using only sunlight, carbon dioxide, and water. Done economically, that would be a huge step toward solving the two outstanding challenges in shifting from fossil fuels to renewable energy: storing large amounts of energy for later use, and powering forms of transportation that cannot easily run on batteries. It would enable solar energy captured during the day to be stored, transported, and used when the sun's not shining. The same fuel could replace fossil fuels that power today's aircraft and ships. "There are no such things as a plug-in electric airplane or ship," says Nate Lewis, the center's founding director.

Hosted at Caltech and Lawrence Berkeley Lab, JCAP was originally funded with $122 million over five years, and its funding was renewed (albeit at a lower level) last year. Now headed by Harry Atwater, a Caltech professor of applied physics, it has made some impressive achievements in its six years of existence. Most notably, JCAP scientists have succeeded in building devices like the one I saw, prototypes that can split water into hydrogen and oxygen at 10 times the efficiency of photosynthesis. That is an important first step to artificial photosynthesis; the next step would be combining hydrogen with carbon dioxide to produce "solar fuels" that could replace fossil fuels.

In the last year, though, JCAP has made a significant shift in direction. The Department of Energy renewed its funding last year at $15 million a year, nearly 40 percent below the rate for the previous

JON HAN

five-year period. What's more, DOE officials instructed the scientists to refocus their efforts away from making devices that could be commercialized in the next several years and toward basic scientific research on the complex processes underlying artificial photosynthesis.

Tackling the underlying scientific challenge of full artificial photosynthesis will require "basic, transformational scientific research and discovery that will

Making solar fuels carbon-neutral will require entirely new technologies.

eventually enable these technologies," says Christopher Fecko, the program manager for JCAP in the DOE's Office of Science. "And we are making excellent progress. Technology deployment and commercial production are in the future."

"In the future" could mean in five years or a few decades. The retreat from hammering out a working solution as fast as possible is an admission that JCAP's original goal of artificial photosynthesis is a lot harder and further off than scientists understood in 2010. It's also a tactical decision not to spend federal money creating a working device to produce hydrogen fuel, even though that technology is much closer to commercialization.

The first step in natural photosynthesis is to split water into hydrogen and oxygen, which is released as a by-product. The hydrogen then reacts with carbon dioxide to produce carbohydrates, which fuel plants' growth. Artificial photosynthesis seeks to use the same inputs—solar energy, water, and carbon dioxide—to produce energy-dense liquid fuels. If those fuels were derived from carbon dioxide captured from air, the process could be carbon-neutral, adding no new emissions of greenhouse gas to the atmosphere.

There are a number of government groups and startups working on bringing artificial photosynthesis to commercialization. The question is, will they bear fruit in time to help limit global climate change? One problem is that making solar fuels carbon-neutral will require entire new technologies and infrastructures to capture carbon from the air or emissions from fossil-fuel plants. The other problem is that converting carbon dioxide to complete the photosynthesis process is very, very hard. It involves six separate chemical steps, and there is no known catalyst that will convert carbon dioxide into fuel efficiently and selectively, the way there is for the water-splitting reaction. JCAP's shift in focus won't get us any closer, in the near term, to actually building devices and creating an industry around solar fuels.

That's why Lewis believes it's a mistake to move away from prototyping and scaling up hydrogen-generating devices. Hydrogen can be burned directly in modified internal-combustion engines, he argues. It can be converted to synthetic fuel via the Fischer-Tropsch process. It can be used in fuel cells to store energy and to produce electricity, leaving only water as a waste product.

The water-splitting prototypes developed at JCAP will still require extensive development to be turned into useful commercial devices. Atwater says other labs and other researchers can bring it to fruition. "Our job is to make research advances that give rise to technology options," he says. "We're scientists—we can't push the ball all the way to the goal line."

In a sense, JCAP is a case study in the promise and the perils of long-term federal funding for energy technologies. Chu speaks ruefully of the road not taken by the program he created. Basic science is a necessary and wonderful thing, he says. "But it's not what I had in mind."

—Richard Martin

QUOTED

"If a single accident means that the developers were reckless, that's a very high bar to set."

— Silvio Savarese, assistant professor at Stanford who specializes in machine vision, on the investigation into Tesla Autopilot's fatal crash.

"We need to boil the ocean, find the genetic populations, and get them on the trials."

— Keith Flaherty, a founder of Strata Oncology, which wants to give free genetic tests to cancer patients to match them to drug studies.

"They'd still be there to feel the roar of the crowd but be watching in a slightly different way."

— Paul Jacobs, vice chairman and co-owner of the Sacramento Kings, on why people would go to a sports arena just to watch via virtual reality.

BY THE NUMBERS

$55 million

Amount the White House is spending this year to create a database of health information to help advance precision medicine.

200 megabytes

Amount of data Microsoft has written into DNA to prove its usefulness for data storage.

$700 million

Amount that Brexit could cost the U.K. annually as a result of uncertainty over energy and climate investments.

$17,000

Price per metric ton of lithium hydroxide, a key mineral for battery storage—nearly triple the price a year ago.

Upfront

A robot in virtual reality appears to experience real impact when punched.

Putting the Physics in VR

A small startup is trying to improve virtual reality by simulating characters' bones and motions more realistically.

Virtual reality can be impressively immersive and realistic, but it's still unusual to have experiences where you really, truly feel you're interacting with digital imagery—to the point that you have a ghostly sense of touching or poking something you know isn't there even as all the visuals point to the contrary. I had one of those rare moments recently as I tried a demo made by a small startup called Midas Touch Games. While wearing an old Oculus developer headset that had a Leap Motion gesture controller attached to its front, I used stick-like virtual hands to play with an animated dog in a way that felt oddly true to life. I could tug at its ears or tail, lift the animal by its front legs, put my fingers in its mouth, and more. And every time I touched the dog with one or both hands, it responded with body movements that were much like what I'd expect from a real furry friend.

Midas Touch made this work by building software meant to properly mimic physics in virtual reality. In the case of the dog demo, for instance, it models the input device (my bare hands) as different bones that can collide with the dog. The dog, too, is modeled with 20 to 30 bones that have mass, shape, and friction, which can collide with my hands. The software uses the force of that impact to figure out which muscles to tighten on the dog.

The startup aims to license its technology to others who can add it to games and other VR applications and create digital images that you can push, ram into each other, and so on, in ways that simulate how these things happen in the real world. The company's cofounder and CEO, Kevin He, thinks this characteristic is essential to making VR feel more lifelike and entrancing.

Evan Suma, a research assistant professor who studies virtual reality at the University of Southern California's Institute for Creative Technologies, says that Midas Touch is getting at one of the key things needed for VR to confer a sense of presence: the illusion of plausibility. "You're no longer a spectator but a participant in the world," he says. *—Rachel Metz*

TO MARKET

Superflex

Robotic Suit

COMPANY:
Superflex

PRICE:
Unknown

AVAILABILITY:
Unknown

Superflex, which spun out of SRI International, is building a wearable robotic suit that may help the elderly ditch their walkers. The current prototype fits over most of the body. It delivers a jolt of supporting power to the legs, arms, or torso when necessary to reduce the burden of a load or correct for the body's shortcomings. Superflex's suit uses a suite of sensors to learn wearers' individual movement styles and safely kicks in power at the exact moment it is needed. As a result, the suit's batteries last much longer than they would if they were fully powering each step or motion. The company is currently looking at options for commercialization. *—Signe Brewster*

Upfront

The People Behind Pebble

Two of the three biggest sums raised on Kickstarter are for the smart-watch pioneer's products. Why do people like them so much?

Startup Pebble raised over $1 million in an hour in May on the crowdfunding website Kickstarter from people eager to get their hands on its latest products. Two of those products are new smart watches with heart-rate sensors, Pebble 2 and Time 2. The third, the Pebble Core—a faceless little square device that's aimed at runners—streams music and tracks your location. By the end of its campaign, Pebble had raked in $12.8 million, the third-biggest haul in Kickstarter's history. This might be impressive for some companies, but for Pebble it's old hat. An earlier version of its smart watch, Pebble Time, snagged $20.3 million last year; the goal had been $500,000.

The Pebble 2 (right), Time 2 (left), and Pebble Core (center) raised over $1 million in an hour on Kickstarter.

Pebble is by no measure a large consumer electronics company, or even a very big smart-watch company; CEO and founder Eric Migicovsky says it had shipped over two million smart watches as of late May, and he estimates that only about 15 percent of sales are through its three crowdfunding campaigns. Technology market researcher IDC ranks Pebble's smart-watch software as the least popular, far behind leaders like Apple's Watch OS and Google's Android Wear. Beyond bringing in over $43 million in Kickstarter money, it has raised only about $15.4 million in venture capital. Yet Pebble has been influential. It helped spur the development of the still small but quickly growing market for smart watches with its original Pebble, which began shipping in early 2013. The market for wearables, driven largely by smart watches and fitness trackers, is expected to climb to 102 million gadgets shipping out this year, according to IDC.

And it has cultivated a loyal fan base in a fickle market where many of the people who buy wrist-worn gadgets quickly toss them in a drawer; plenty of the people backing its latest Kickstarter campaign, for instance, have done so in the past, too. So what is it about the company that keeps customers coming back, watch after watch? Pebble owners say it's a combination of factors, including its price, which currently ranges from $100 to $250, depending on the watch and band. There's also its long battery life relative to other smart watches—a maximum of seven or 10 days on most models, helped by a low-power e-paper display, compared with roughly a day for many competitors—and its ease of use.

"It doesn't feel like an extra piece of technology I have to take care of," says Jana Maiuri, a teacher in Oakland, California, who has bought three Pebble watches and backed its latest Kickstarter. She likes that the device's display stays on all the time so she can easily check the time. This isn't the case with a lot of other smart watches, which rely on the more consumptive displays also seen in smartphones. And while many smart watches tout touch screens as a convenient way to use the diminutive hardware, she prefers Pebble's decision thus far to eschew touch displays in favor of buttons on the side of the watch. This way, she says, she doesn't have to even look at her wrist when, say, adjusting music or changing slides on a projector in her classroom.

Pebble almost certainly has a rocky road ahead of it, though. IDC expects it to ship less than 500,000 smart watches this year, and less than 600,000 in 2020. If the markets for smart watches and wearables in general continue to grow apace, that will mean Pebble has a much smaller slice of the pie.

Migicovsky, meanwhile, is staying upbeat. The company has staked a claim in the smart-watch market, he says, and increasing competition has helped it focus. "We're not in it for the short win, just to make a quick gadget and get out," he says. *—Rachel Metz*

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AI's Unspoken Problem

Extraordinary progress has been made in artificial intelligence of late. But to achieve their full promise, machines must understand language, and that will be the most difficult step yet.

By Will Knight

About halfway through a particularly tense game of Go held in Seoul, South Korea, between Lee Sedol, one of the best players of all time, and AlphaGo, an artificial intelligence created by Google, the AI program made a mysterious move that demonstrated an unnerving edge over its human opponent.

On move 37, AlphaGo chose to put a black stone in what seemed, at first, like a ridiculous position. It looked certain to give up substantial territory—a rookie mistake in a game that is all about controlling the space on the board. Two television commentators wondered if they had misread the move or if the machine had malfunctioned somehow. In fact, contrary to any conventional wisdom, move 37 would enable AlphaGo to build a formidable foundation in the center of the board. The Google program had effectively won the game using a move that no human would've come up with.

AlphaGo's victory is particularly impressive because the ancient game of Go is often looked at as a test of intuitive intelligence. The rules are quite simple. Two players take turns putting black or white stones at the intersection of horizontal and vertical lines on a board, trying to surround their opponent's pieces and remove them from play. Playing well, however, is incredibly hard.

Whereas chess players are able to look a few moves ahead, in Go this isn't possible without the game unfolding into intractable complexity, and there are no classic gambits. There is also no straightforward way to measure advantage, and it can be hard for even an expert player to explain precisely why he or she made a particular move. This makes it impossible to write a simple set of rules for an expert-level computer program to follow.

AlphaGo wasn't told how to play Go at all. Instead, the program analyzed hundreds of thousands of games and played millions of matches against itself. Among several AI techniques, it used an increasingly popular method known as deep learning, which involves mathematical calculations inspired, very loosely, by the way interconnected layers of neurons fire in a brain as it learns to make sense of new information. The program taught itself through hours of practice, gradually honing an intuitive sense of strategy. That it was then able to beat one of the world's best Go players represents a true milestone in machine intelligence and AI.

A few hours after move 37, AlphaGo won the game to go up two games to nothing in the best-of-five match. Afterward Sedol stood before a crowd of journalists and photographers, politely apologizing for letting humankind down. "I am quite speechless," he said, blinking through a storm of flash photography.

AlphaGo's surprising success points to just how much progress has been made in artificial intelligence over the last few years, after decades of frustration and setbacks often described as an

Mel Bochner
Babble
2011

One reason that understanding language is so difficult for computers and AI systems is that words often have meanings based on context and even the appearance of the letters and words. In the following pages, several artists demonstrate the use of a variety of visual clues to convey meanings far beyond the actual letters.


BABBLE, BLATH-
ER, BLABBER, BIL-
GE, BLARNEY, BUNK,
BLUFF, BLUSTER,
BOSH, BULLSHIT,
JIVE, JARGON, DRI-
VEL, DROOL, RUN-
NING OFF AT THE
MOUTH, TALKING
TRASH, SHOOT-
IN THE HIT, ETC,
ETC, AD NAUSEUM,

"AI winter." Deep learning means that machines can increasingly teach themselves how to perform complex tasks that only a couple of years ago were thought to require the unique intelligence of humans. Self-driving cars are already a foreseeable possibility. In the near future, systems based on deep learning will help diagnose diseases and recommend treatments.

Yet despite these impressive advances, one fundamental capability remains elusive: language. Systems like Siri and IBM's Watson can follow simple spoken or typed commands and answer basic questions, but they can't hold a conversation and have no real understanding of the words they use. If AI is to be truly transformative, this must change.

Even though AlphaGo cannot speak, it contains technology that might lead to greater language understanding. At companies such as Google, Facebook, and Amazon, as well as at leading academic AI labs, researchers are attempting to finally solve that seemingly intractable problem, using some of the same AI tools—including deep learning—that are responsible for AlphaGo's success and today's AI revival. Whether they succeed will determine the scale and character of what is turning into an artificial-intelligence revolution. It will help determine whether we have machines we can easily communicate with—machines that become an intimate part of our everyday life—or whether AI systems remain mysterious black boxes, even as they become more autonomous. "There's no way you can have an AI system that's humanlike that doesn't have language at the heart of it," says Josh Tenenbaum, a professor of cognitive science and computation at MIT. "It's one of the most obvious things that set human intelligence apart."

Perhaps the same techniques that let AlphaGo conquer Go will finally enable computers to master language, or perhaps something else will also be required. But without language understanding, the impact of AI will be different. Of course,

PHOTO BY CATHY CARVER; COURTESY OF MOVED PICTURES ARCHIVE;

we can still have immensely powerful and intelligent software like AlphaGo. But our relationship with AI may be far less collaborative and perhaps far less friendly. "A nagging question since the beginning was 'What if you had things that were intelligent in the sense of being effective, but not like us in the sense of not empathizing with what we are?'" says Terry Winograd, a professor emeritus at Stanford University. "You can imagine machines that are not based on human intelligence, which are based on this big-data stuff, and which run the world."

Machine whisperers

A couple of months after AlphaGo's triumph, I traveled to Silicon Valley, the heart of the latest boom in artificial intelligence. I wanted to visit the researchers who are making remarkable progress on practical applications of AI and who are now trying to give machines greater understanding of language.

I started with Winograd, who lives in a suburb nestled into the southern edge of Stanford's campus in Palo Alto, not far from the headquarters of Google, Facebook, and Apple. With curly white hair and a bushy mustache, he looks the part of a venerable academic, and he has an infectious enthusiasm.

Back in 1968, Winograd made one of the earliest efforts to teach a machine to talk intelligently. A math prodigy fascinated with language, he had come to MIT's new AI lab to study for his PhD, and he decided to build a program that would converse with people, via a text prompt, using everyday language. It didn't

Lawrence Weiner
A Rubber Ball Thrown on the Sea
1970 / 2014


PURE BEAUTY

John Baldessari
Pure Beauty
1966–68

seem an outlandish ambition at the time. Incredible strides were being made in AI, and others at MIT were building complex computer vision systems and futuristic robot arms. "There was a sense of unknown, unbounded possibilities," he recalls.

Not everyone was convinced that language could be so easily mastered, though. Some critics, including the influential linguist and MIT professor Noam Chomsky, felt that the AI researchers would struggle to get machines to understand, given that the mechanics of language in humans were so poorly understood. Winograd remembers attending a party where a student of Chomsky's walked away when he heard him say that he worked in the AI lab.

But there was reason to be optimistic, too. Joseph Weizenbaum, a German-born professor at MIT, had built the very first chatbot program a couple of years earlier. Called ELIZA, it was programmed to act like a cartoon psychotherapist, repeating key parts of a statement or asking questions to encourage further conversation. If you told the program you were angry at your mother, for instance, it would say, "What else comes to mind when you think about your mother?" A cheap trick, but it worked surprisingly well. Weizenbaum was shocked when some subjects began confessing their darkest secrets to his machine.

Winograd wanted to create something that really seemed to understand language. He began by reducing the scope of the problem. He created a simple virtual environment, a "block world," consisting of a handful of imaginary objects sitting on an imaginary table. Then he created a program, which he named SHRDLU, that was capable of parsing all the nouns, verbs, and simple rules of grammar needed to refer to this stripped-down virtual world. SHRDLU (a nonsense word formed by the second column of keys on a Linotype machine) could describe the objects, answer questions about their relationships, and make changes to the block world in response to typed commands. It even had a kind of memory, so that if you told it to move "the red cone" and then later referred to "the cone," it would assume you meant the red one rather than one of another color.

SHRDLU was held up as a sign that the field of AI was making profound progress. But it was just an illusion. When Winograd tried to make the program's block world larger, the rules required to account for the necessary words and grammatical complexity became unmanageable. Just a few years later, he had given up, and eventually he abandoned AI altogether to focus on other areas of research. "The limitations were a lot closer than it seemed at the time," he says.

Winograd concluded that it would be impossible to give machines true language understanding using the tools available then. The problem, as Hubert Dreyfus, a professor of philosophy at UC Berkeley, argued in a 1972 book called *What Computers Can't Do*, is that many things humans do require a kind of instinctive intelligence that cannot be captured with hard-and-fast rules. This is precisely why, before the match between Sedol and AlphaGo, many experts were dubious that machines would master Go.

But even as Dreyfus was making that argument, a few researchers were, in fact, developing an approach that would eventually give machines this kind of intelligence. Taking loose inspiration from neuroscience, they were experimenting with artificial neural networks—layers of mathematically simulated neurons that could be trained to fire in response to certain inputs. To begin with, these systems were painfully slow, and the approach was dismissed as impractical for logic and reasoning. Crucially, though, neural networks could learn to do things that couldn't be hand-coded, and later this would prove useful for simple tasks such as recognizing handwritten characters, a skill that was commercialized in the 1990s for reading the numbers on checks. Proponents maintained that neural networks would eventually let machines to do much, much more. One day, they claimed, the technology would even understand language.

Over the past few years, neural networks have become vastly more complex and powerful. The approach has benefited from key mathematical refinements and, more important, faster computer hardware and oodles of data. By 2009, researchers at the University of Toronto had shown that a many-layered deep-learning network could recognize speech with record accuracy. And then in 2012, the same group won a machine-vision contest using a deep-learning algorithm that was astonishingly accurate.

A deep-learning neural network recognizes objects in images using a simple trick. A layer of simulated neurons receives input in the form of an image, and some of those neurons will fire in response to the intensity of individual pixels. The resulting signal passes through many more layers of interconnected neurons before reaching an output layer, which signals that the object has been seen. A mathematical tech-

nique known as backpropagation is used to adjust the sensitivity of the network's neurons to produce the correct response. It is this step that gives the system the ability to learn. Different layers inside the network will respond to features such as edges, colors, or texture. Such systems can now recognize objects, animals, or faces with an accuracy that rivals that of humans.

There's an obvious problem with applying deep learning to language. It's that words are arbitrary symbols, and as such they are fundamentally different from imagery. Two words can be similar in meaning while containing completely different letters, for instance; and the same word can mean various things in different contexts.

In the 1980s, researchers had come up with a clever idea about how to turn language into the type of problem a neural network can tackle. They showed that words can be represented as mathematical vectors, allowing similarities between related words to be calculated. For example, "boat" and "water" are close in vector space even though they look very different. Researchers at the University of Montreal, led by Yoshua Bengio, and another group at Google, have used this insight to build networks in which each word in a sentence can be used to construct a more complex representation—something that Geoffrey Hinton, a professor at the University of Toronto and a prominent deep-learning researcher who works part-time at Google, calls a "thought vector."

By using two such networks, it is possible to translate between two languages with excellent accuracy. And by combining this type of network with one designed to recognize objects in images, it is possible to conjure up surprisingly plausible captions.

The purpose of life

Sitting in a conference room at the heart of Google's bustling headquarters in Mountain View, California, one of the company's researchers who helped develop this approach, Quoc Le, is contemplating the idea of a machine that could hold a proper conversation. Le's ambitions cut right to the heart of why talking machines could be useful. "I want a way to simulate thoughts in a machine," he says. "And if you want to simulate thoughts, then you should be able to ask a machine what it's thinking about."

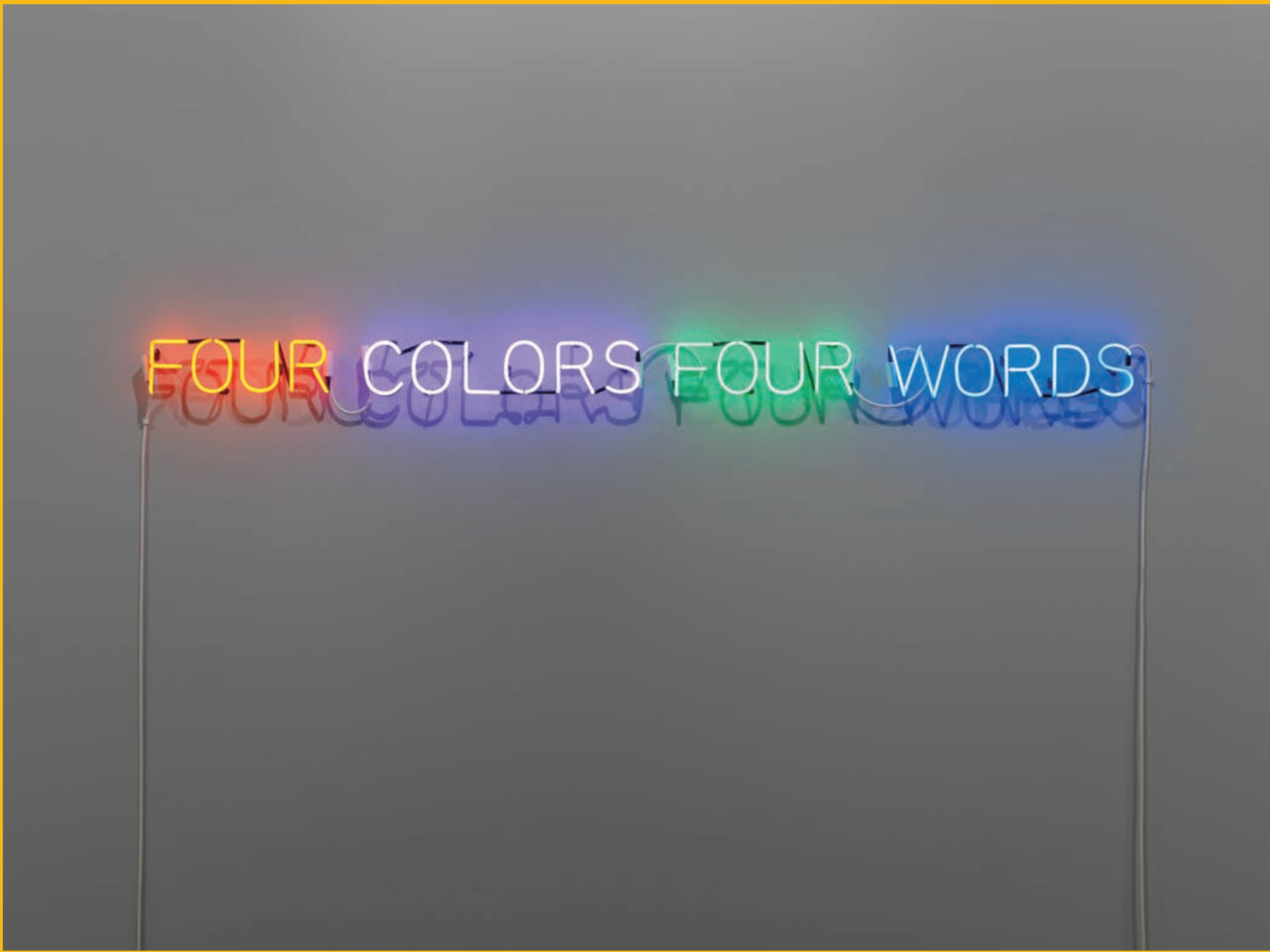
Google is already teaching its computers the basics of language. This May the company announced a system, dubbed Parsey McParseface, that can look at syntax, recognizing nouns, verbs, and other elements of text. It isn't hard to see how valuable better language understanding could be to the company. Google's search algorithm used to simply track keywords and links between Web pages. Now, using a system called RankBrain, it reads the text on pages in an effort to glean meaning and deliver better results. Le wants to take that much further. Adapting the system that's proved useful in translation and image captioning, he and his colleagues built Smart Reply, which reads the contents of Gmail messages and suggests a handful of possible replies. He also created a program that learned from Google's IT support chat logs how to answer simple technical queries.

Most recently, Le built a program capable of producing passable responses to open-ended questions; it was trained by being fed dialogue from 18,900 movies. Some of its replies seem eerily spot-on. For example, Le asked, "What is the purpose of life?" and the program responded, "To serve the greater good." "It was a pretty good answer," he remembers with a big grin. "Probably better than mine would have been."

There's only one problem, as quickly becomes apparent when you look at more of the system's answers. When Le asked, "How many legs does a cat have?" his system answered, "Four, I think." Then he tried, "How many legs does a centipede have?" which produced a curious response: "Eight." Basically, Le's program has no idea what it's talking about. It understands that certain combinations of symbols go together, but it has no appreciation of the real world. It doesn't know what a centipede actually looks like, or how it moves. It is still just an illusion of intelligence, without the kind of common sense that humans take for granted. Deep-learning systems can often be wonky this way. The one Google created to generate captions for images would make bizarre errors, like describing a street sign as a refrigerator filled with food.

By a curious coincidence, Terry Winograd's next-door neighbor in Palo Alto is someone who might be able to help computers attain a deeper appreciation of what words actually mean. Fei-Fei Li, director of the Stanford Artificial Intelligence Lab, was on maternity leave when I visited, but she invited me to her home and proudly introduced me to her beautiful three-month-old baby, Phoenix. "See how she looks at you more than me," Li said as Phoenix stared at me. "That's because you are new; it's early facial recognition."

Li has spent much of her career researching machine learning and computer vision. Several years ago, she led an effort to build a database of millions of images of objects, each tagged with an appropriate keyword. But Li believes machines need an even more sophisticated understanding of what's happening in the world, and this year her team released another database of images, annotated in much richer detail. Each image has been tagged by a human with dozens of descriptors: "A dog riding a skateboard," "Dog has fluffy, wavy fur," "Road is cracked," and so on. The hope is that machine-learning systems will learn to understand more about the physical world. "The language part of the brain gets fed a lot of information, including from the visual system," Li says. "An important part of AI will be integrating these systems."



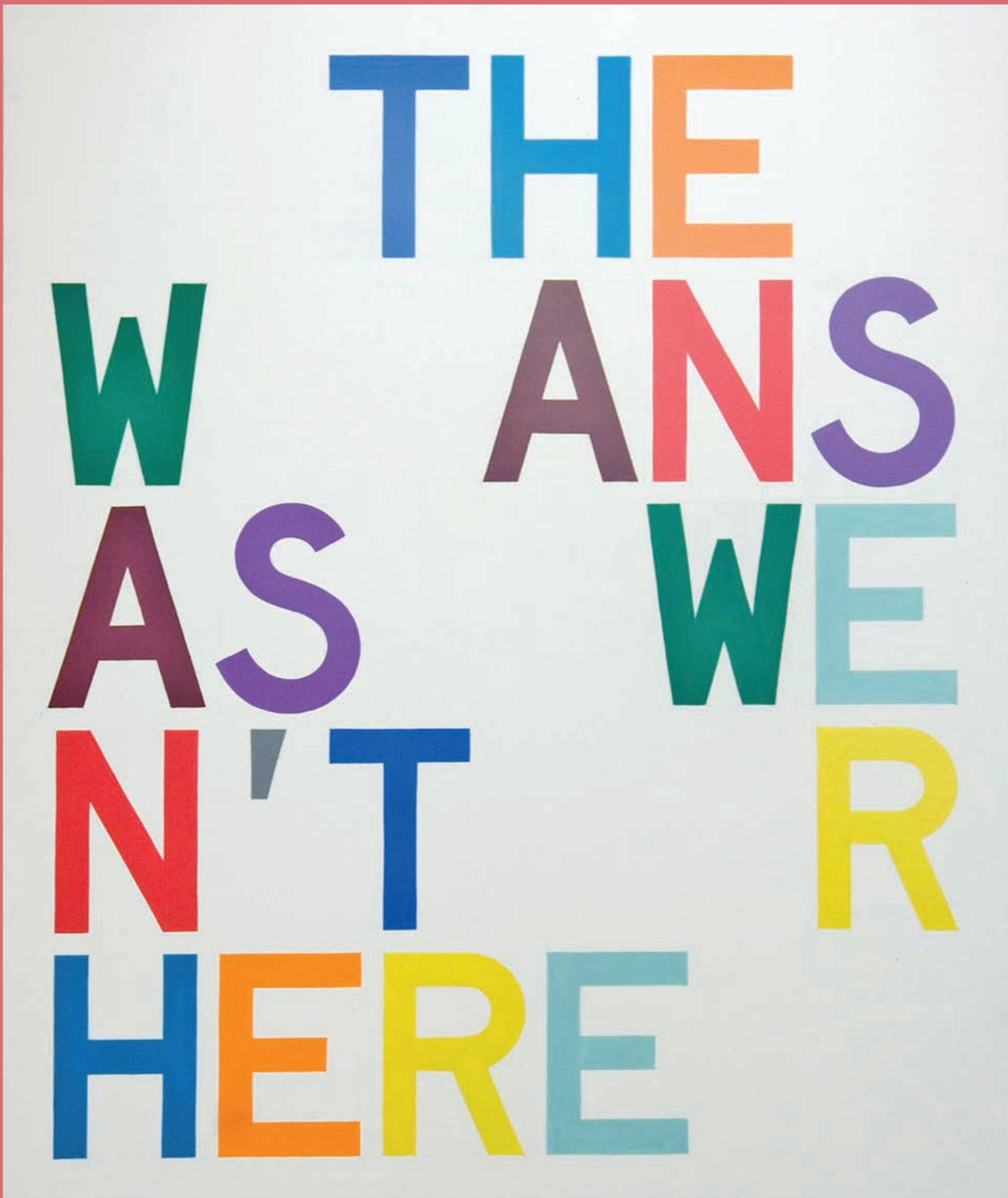
Joseph Kosuth
Four Colors Four Words
1966

This is closer to the way children learn, by associating words with objects, relationships, and actions. But the analogy with human learning goes only so far. Young children do not need to see a skateboarding dog to be able to imagine or verbally describe one. Indeed, Li believes that today's machine-learning and AI tools won't be enough to bring about real AI. "It's not just going to be data-rich deep learning," she says. Li believes AI researchers will need to think about things like emotional and social intelligence. "We [humans] are terrible at computing with huge data," she says, "but we're great at abstraction and creativity."

No one knows how to give machines those human skills—if it is even possible. Is there something uniquely human about such qualities that puts them beyond the reach of AI?

Cognitive scientists like MIT's Tenenbaum theorize that important components of the mind are missing from today's neural networks, no matter how large those networks might be. Humans have the ability to learn very quickly from a relatively small amount of data and have a built-in ability to model the world in 3-D very efficiently. "Language builds on other abilities that are probably more basic, that are present in young infants before they have language: perceiving the world visually, acting on our motor systems, understanding the physics of the world or other agents' goals," Tenenbaum says.

If he is right, then it will be difficult to re-create language understanding in machines and AI systems without trying to mimic human learning, mental model building, and psychology.


THE
W ANS
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Tauba Auerbach
The Answer/ Wasn't Here II
2008

Explain yourself

Noah Goodman's office in Stanford's psychology department is practically bare except for a couple of abstract paintings propped against one wall and a few overgrown plants. When I arrived, Goodman was typing away on a laptop, his bare feet up on a table. We took a stroll across the sun-bleached campus for iced coffee. "Language is special in that it relies on a lot of knowledge about language but it also relies on a huge amount of common-sense knowledge about the world, and those two go together in very subtle ways," he explained.

Goodman and his students have developed a programming language, called Webppl, that can be used to give computers a kind of probabilistic common sense, which turns out to be pretty useful in a conversation. One experimental version can understand puns, and another can cope with hyperbole. If it is told that some people had to wait "forever" for a table in a restaurant, it will automatically decide that the literal meaning is improbable, and they most likely just hung around for a long time and were annoyed. The system is far from truly intelligent, but it shows how new approaches could help make AI programs that talk in a more lifelike way.

At the same time, Goodman's example also suggests just how difficult it will be to teach language to machines. Understanding the contextual meaning of "forever" is the kind of thing that AI systems will need to learn, but it is a rather simple and rudimentary accomplishment.

Still, despite the difficulty and complexity of the problem, the startling success that researchers have had using deep-learning techniques to recognize images and excel at games like Go does at least provide hope that we might be on the verge of breakthroughs in language, too. If so, those advances will come just in time. If AI is to serve as a ubiquitous tool that people use to augment their own intelligence and trust to take over tasks in a seamless collaboration, language will be key. That will be especially true as AI systems increasingly use deep learning and other techniques to essentially program themselves.

"In general, deep-learning systems are awe-inspiring," says John Leonard, a professor at MIT who researches automated driving. "But on the other hand, their performance is really hard to understand."

Toyota, which is studying a range of self-driving technologies, has initiated a research project at MIT led by Gerald Sussman, an expert on artificial intelligence and programming language, to develop automated driving systems capable of explaining why they took a particular action. And an obvious way for a self-driving car to do this would be by talking. "Building systems that know what they know is a really hard problem," says Leonard, who is leading a different Toyota-backed project at MIT. "But yeah, ideally they would give not just an answer but an explanation."

A few weeks after returning from California, I saw David Silver, the Google DeepMind researcher who designed AlphaGo, give a talk about the match against Sedol at an academic conference in New York. Silver explained that when the program came up with its killer move during game two, his team was just as surprised as everyone else. All they could see was AlphaGo's predicted odds of winning, which changed little even after move 37. It was only several days later, after careful analysis, that the Google team made a discovery: by digesting previous games, the program had calculated the chances of a human player making the same move at one in 10,000. And its practice games had also shown that the play offered an unusually strong positional advantage.

So in a way, the machine knew that Sedol would be completely blindsided.

Silver said that Google is considering several options for commercializing the technology, including some sort of intelligent assistant and a tool for health care. Afterward, I asked him about the importance of being able to communicate with the AI behind such systems. "That's an interesting question," he said after a pause. "For some applications it may be important. Like in health care, it may be important to know why a decision is being made."

Indeed, as AI systems become increasingly sophisticated and complex, it is hard to envision how we will collaborate with them without language—without being able to ask them, "Why?" More than this, the ability to communicate effortlessly with computers would make them infinitely more useful, and it would feel nothing short of magical. After all, language is our most powerful way of making sense of the world and interacting with it. It's about time that our machines caught up.

Will Knight is senior editor for AI and robotics at MIT Technology Review. *His feature "The People's Robots" appeared in the May/June issue.*

Fail-Safe Nuclear Power

Cheaper and cleaner nuclear plants could finally become reality—but not in the United States, where the technology was invented more than 50 years ago.

By Richard Martin

EDWIN FOTHERINGHAM

In February I flew through the interior of a machine that could represent the future of nuclear power. I was on a virtual-reality tour at the Shanghai Institute of Applied Physics in China, which plans in the next few years to build an experimental reactor whose design makes a meltdown far less likely. Inside the core—a superhot, intensely radioactive place where no human will ever go—the layers of the power plant peeled back before me: the outer vessel of stainless steel, the inner layer of a high-tech alloy, and finally the nuclear fuel itself, tens of thousands of billiard-ball-size spheres containing particles of radioactive material.

Given unprecedented access to the inner workings of China's advanced nuclear R&D program, I was witnessing a new nuclear technology being born. Through the virtual reactor snaked an intricate system of pipes carrying the fluid that makes this system special: a molten salt that cools the reactor and carries

heat to drive a turbine and make electricity. At least in theory, this type of reactor can't suffer the kind of catastrophic failure that happened at Chernobyl and Fukushima, making unnecessary the expensive and redundant safety systems that have driven up the cost of conventional reactors. What's more, the new plants should produce little waste and might even eat up existing nuclear waste. They could run on uranium, which powers 99 percent of the nuclear power plants in the world, or they could eventually run on thorium, which is cleaner and more abundant. The ultimate goal of the Shanghai Institute: to build a molten-salt reactor that could replace the 1970s-era technology in today's nuclear power plants and help wean China off the coal that fouls the air of Shanghai and Beijing, ushering in an era of cheap, abundant, zero-carbon energy.

Over the next two decades China hopes to build the world's largest nuclear power industry. Plans include as many as 30 new conventional nuclear plants (in addition to the 34 reactors operating today) as well as a variety of next-generation reactors, including thorium molten-salt reactors, high-temperature gas-cooled reactors (which, like molten-salt reactors, are both highly efficient and inherently safe), and sodium-cooled fast reactors (which can consume spent fuel from conventional reactors to make electricity). Chinese planners want not only to dramatically expand the country's domestic nuclear capacity but also to become the world's leading supplier of nuclear reactors and components, a prospect that many Western observers find alarming.

The Shanghai Institute's effort to develop molten-salt reactors, a technology that has sat all but forgotten in the United States for decades, reflects just how daring China's nuclear ambitions are. Already, the government has invested some two billion Chinese renminbi ($300 million) over the last five years in molten-salt R&D. Building actual plants will require tens of billions more. As with other innovative nuclear technologies in development around the world, there are few guarantees: though people have run small, experimental molten-salt reactors, no one's ever actually built one at utility scale and hooked it up to the grid. Yet the Chinese government expects to have a commercial-size plant up and running within 15 years, helping to revive the beleaguered nuclear power industry.

The first experiments with molten-salt reactors were carried out at Oak Ridge National Laboratory, in Tennessee, under its director Alvin Weinberg in the late 1950s. Today's Chinese program, in fact, is the fruit of a unique and somewhat controversial partnership between Oak Ridge and the Shanghai Institute. The U.S. research program went on for more than a decade but was eventually shut down in favor of the technology used in the vast majority of nuclear power plants today. In retrospect, that decision contributed not only to the demise of a promising nuclear technology but also to the long stagnation of the industry.

Today, though, the world needs nuclear energy more than ever if we are to limit climate change. According to the International Energy Agency, the world's nuclear capacity needs to more than double by midcentury if we are to stay within 2 °C of warming. As it stands now, that seems unlikely. Several countries, including China and India, have embarked on massive nuclear power build-outs, but most will entail big, conventional reactors—technology that is too expensive for much of the rest of the world. Even countries, such as Germany, that can afford nuclear power are phasing it out because they fear another disaster. That makes the fail-safe nuclear power plants being developed at the Shanghai Institute of paramount urgency.

The world needs nuclear energy more than ever if we are to limit climate change.

Nuclear Time Line

Molten-salt reactors have been stuck on the drawing board even as conventional nuclear power technology stalled.

1942
An experimental reactor built by Enrico Fermi and his team at the University of Chicago produces the first controlled nuclear chain reaction.

1957
The Shippingport nuclear plant, the first full-scale reactor to supply electricity to the grid, starts up in Pennsylvania. It will run until 1982.

1965–69
Scientists at Oak Ridge National Laboratory run an experimental molten-salt reactor. The program will be formally canceled in 1973.

1979
A cooling malfunction causes a partial meltdown at Three Mile Island in Pennsylvania, bringing new reactor construction in the U.S. to a standstill.

COURTESY OF OAK RIDGE NATIONAL LABORATORY, (1965); COURTESY OF METROPOLITAN EDISON COMPANY/ REPORT OF THE PRESIDENT'S COMMISSION ON THE ACCIDENT AT THREE MILE ISLAND (1979)

1983
An effort to develop a new nuclear power technology, the Clinch River breeder reactor program, is canceled after consuming more than $1 billion. No prototype or demonstration reactor was ever built.

1986
The worst nuclear disaster in history occurs at the Chernobyl plant in Ukraine, furthering the anti-nuclear movement of the 1980s and 1990s.

1996
Unit No. 1 at the Watts Bar plant, in Tennessee, begins producing power. It will be the last new nuclear reactor to come online in the United States until 2016, when a second unit at Watts Bar starts up.

2011
An earthquake and tsunami cause a coolant failure and fuel meltdown at the Fukushima-Daiichi nuclear power station in Japan. That leads several countries to start phasing out nuclear plants.

2011
The Oak Ridge National Laboratory signs an agreement with the Chinese Academy of Sciences to develop molten-salt reactors.

HERIBERT PROEPPER/AP (1986); YASUSHI KANNO/AP (2011); COURTESY OF SHANGHAI INSTITUTE OF APPLIED PHYSICS (2012)

After my virtual tour, Kun Chen, one of the molten-salt program's lead scientists, walked me back to the institute's main administration building. Snow had fallen overnight, and it was bitterly cold. In the auditorium a small crowd of staffers had gathered for a talk by Xu Hongjie, the director of the molten-salt program. It was the week before the long lunar new year holiday, and the institute's annual banquet was being held that night. Xu spoke for more than two hours about the history of molten-salt technology and its prospects for the future.

"This has been China's dream for a half-century," he said. "Previously, we lacked the necessary knowledge and skills to make it a reality. Now we have the resources and the technology and the expertise. Now we can do it."

Chain reactions

Alvin Weinberg first came to Oak Ridge in 1945, just after its laboratories had been built in the northern Tennessee hills to make weapons-grade uranium and plutonium. A veteran of the Manhattan Project, Weinberg became director of the rapidly growing national lab in 1955 and held the position until 1973. He was a pioneering nuclear physicist and a philosopher of nuclear power who used the phrase "Faustian bargain" to describe the tension between industrialized society's thirst for abundant energy and the extreme vigilance needed to keep nuclear power safe. To make this energy source both clean and extremely cheap, he believed, the link between nuclear power and nuclear weapons would have to be severed. And the way to break that link was the thorium molten-salt reactor.

Under Weinberg's leadership, a team of enthusiastic young chemists, physicists, and engineers operated a small, experimental molten-salt reactor from 1965 to 1969. That reactor at Oak Ridge ran on uranium; Weinberg's eventual goal was to build one that would run exclusively on thorium, which, unlike uranium, cannot easily be made into a bomb. But the molten-salt experiment was abandoned in the early 1970s. One big reason was that Weinberg managed to alienate his superiors by warning of the dangers of conventional nuclear power at a time when dozens of such reactors were already under construction or in the planning stages.

By the end of the century, the U.S. had built 104 nuclear reactors, but construction of new ones had all but come to a halt, and the technology remained stuck in the 1970s. Because conventional reactors require huge, costly containment vessels that can blow up in extreme conditions, and because they use extensive external cooling systems to make sure the solid-fuel core doesn't overheat and cause a runaway reaction leading to a meltdown, they are hugely expensive. Two new reactors being built now in Georgia could cost $21 billion, 50 percent over the original estimate of $14 billion. All that for 40-year-old technology.

Today, though, as climate change accelerates and government officials and scientists seek a nuclear technology without the expensive problems that have stalled the conventional version, molten salt is enjoying a renaissance. Companies such as Terrestrial Energy, Transatomic Power, Moltex, and Flibe Energy are vying to develop new molten-salt reactors. Research programs on various forms

of the technology are under way at universities and institutes in Japan, France, Russia, and the United States, in addition to the one at the Shanghai Institute. Besides the work going into developing solid-fuel reactors that are cooled by molten salt (like the one I toured virtually in Shanghai), there are even more radical designs that also use radioactive materials dissolved in molten salt as the fuel (as Weinberg's experiment did).

Like all nuclear plants, molten-salt reactors excite atoms in a radioactive material to create a controlled chain reaction. The reaction unleashes heat that boils water, creating steam that drives a turbine to generate electricity. Solid-fuel reactors cooled with molten salt can run at higher temperatures than conventional reactors, making them more efficient, and they operate at atmospheric pressures—meaning they do not require expensive vessels of the sort that ruptured at Chernobyl. Molten-salt reactors that use liquid fuel have an even more attractive advantage: when the temperature in the core reaches a certain threshold, the liquid expands, which slows the nuclear reactions and lets the core cool. To take advantage of this property, the reactor is built like a bathtub, with a drain plug in the bottom; if the temperature in the core gets too high, the plug melts and the fuel drains into a shielded tank, typically underground, where it is stored safely as it cools. These reactors should be able to tap more of the energy available in radioactive material than conventional ones do. That means they should dramatically reduce the amount of nuclear waste that must be handled and stored.

Because they don't require huge containment structures and need less fuel to produce the same amount of electricity, these reactors are more compact than today's nuclear plants. They could be mass-produced, in factories, and combined in arrays to form larger power plants.

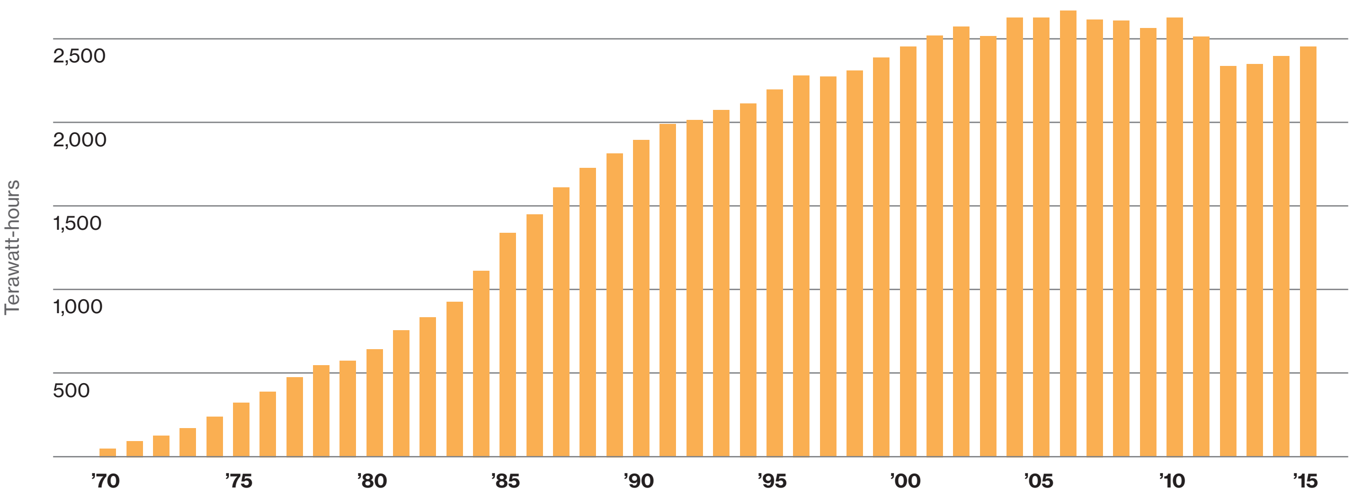
All of that should make them cheaper to build. Unlike wind and solar, which have gotten far less expensive over time, nuclear plants have become much more so. According to the U.S. Energy Information Administration, the inflation-adjusted cost of building a nuclear plant rose from $1,500 per kilowatt of capacity in the early 1960s to more than $4,000 a kilowatt by the mid-1970s. In its latest calculation, in 2013, the EIA found that the figure had risen to more than $5,500—more expensive than a solar power plant or onshore wind farm, and far more than a natural-gas plant. That up-front cost is amplified by the large size of the reactors; at the average cited by the EIA, a one-gigawatt plant would cost $5.5 billion, a risky investment for any company.

Those up-front costs are balanced by the fact that nuclear plants are relatively cheap to operate: at new plants the levelized cost of electricity, which measures the cost of power generated over the lifetime of the plant, is $95 per megawatt-hour, according to the EIA—comparable to the cost of electricity from coal-fired plants, and less than solar power ($125 a megawatt-hour). Still, natural-gas plants are far cheaper to build, and the cost of the electricity they produce ($75 a megawatt-hour, according to the EIA) is also lower. Tightening regulations on carbon emissions makes nuclear more attractive, but lowering the cost of construction is critical to the future of zero-carbon nuclear power.

That is the pitch being made by a new crop of startups working on advanced nuclear reactors, several of them funded by Silicon Valley investors. Transatomic Power, for instance, was founded by a pair of MIT PhDs, Leslie Dewan and Mark Massie, who have designed a 520-megawatt plant (about the size of an average coal plant today) that they think can be built for $2 billion, or $3,846 per kilowatt of capacity. That is in line with the cost of building a solar power plant—

Nuclear Energy Worldwide

The production of electricity from nuclear power plants is down from a peak reached in the last decade.



DATA FROM WORLD NUCLEAR ASSOCIATION

but would have the huge advantage of being able to produce power continuously, not just when the sun shines. Terrestrial Energy, which recently won a research grant from the Canadian government to build a prototype reactor, says that its molten-salt reactor could eventually be built for as little as $2,000 a kilowatt.

But even though molten-salt designs have energized inventive young technologists, getting a novel nuclear power technology licensed and built in the U.S. remains a daunting prospect. Simply applying for a license from the Nuclear Regulatory Commission can take years and cost hundreds of millions of dollars, which is why some of these startups may never get off the ground. What's more, even $2 billion would be a lot of money for investors and utilities to spend on an unproven technology with questionable financial advantages. Which is why the program closest to producing a working reactor is in the People's Republic of China.

Think big

Even as the original experiment with molten-salt technology was winding down in the U.S. in the 1970s, a small group of researchers at the Shanghai Institute of Applied Physics, part of the Chinese Academy of Sciences, was launching its own investigation into thorium-fueled molten-salt reactors. But China, which would not start up its first nuclear power plant until 1991, lacked the expertise and the money to develop the sophisticated machinery and expensive materials in advanced reactors. By the 21st century, like all other countries with nuclear power, China relied on conventional reactors. But the embers of the concept still glowed in the minds of Chinese nuclear scientists.

From the Chinese point of view, thorium has a particular advantage: while mainland China has a small percentage of the world's uranium, it has plenty of thorium. Having an abundant source of carbon-free energy would solve several of China's energy dilemmas at one go. "In the eyes of the central government, we are not here to do mature technologies—we have to create something new, something strategic," says Kun Chen, the molten-salt scientist who led my virtual tour in Shanghai. "You have to think big."

Educated at the prestigious University of Science and Technology of China, in Hefei, Chen earned a PhD from Indiana University and worked for several years at Argonne National Laboratory (which, like Oak Ridge, is part of the U.S. Department of Energy). But he came back to China to build a world-changing reactor.

He heard about it in 2009, when he visited Shanghai to present a seminar at the Institute of Applied Physics. A scientist there told him about the thorium molten-salt reactor—a project not yet funded or announced. "Our team got most of the technical documents from the Web—they were posted by the Oak Ridge team," recalls Xu Hongjie, the director of the molten-salt program, shaking his head in either admiration or amazement at the openness of the Americans. "They posted everything there for free."

At Xu's urging, Chen joined the Shanghai Institute in 2010, and today he is in charge of collaborating with Oak Ridge. The U.S. lab is contributing research on materials, control systems, and computer simulations to the project and has built a large molten-salt testing facility that was funded by the Chinese Academy of Sciences. While some scientists and nuclear-power advocates vehemently oppose the idea of helping China build a world-leading nuclear industry, many Oak Ridge engineers are just eager to see molten-salt reactors built somewhere. "One of the important things to realize is that a number of key people in molten-salt reactors are retiring very fast or passing away," says David Holcombe, who heads Oak Ridge's collaboration with the Shanghai Institute. "You can't just import a new set of staff if we're going to maintain this capability. China is providing the funding that allows us to transfer that knowledge, to gain practical experience at building and operating these reactors."

To start, the Shanghai Institute plans to take a hybrid approach, using molten salt to cool a solid-fuel core similar to the ones in conventional nuclear plants. Then, Chen says, the team will progress to liquid fuels to fully realize the technology's potential for safety and efficiency. At first the fuel will be uranium, but the Chinese engineers plan to shift later to thorium.

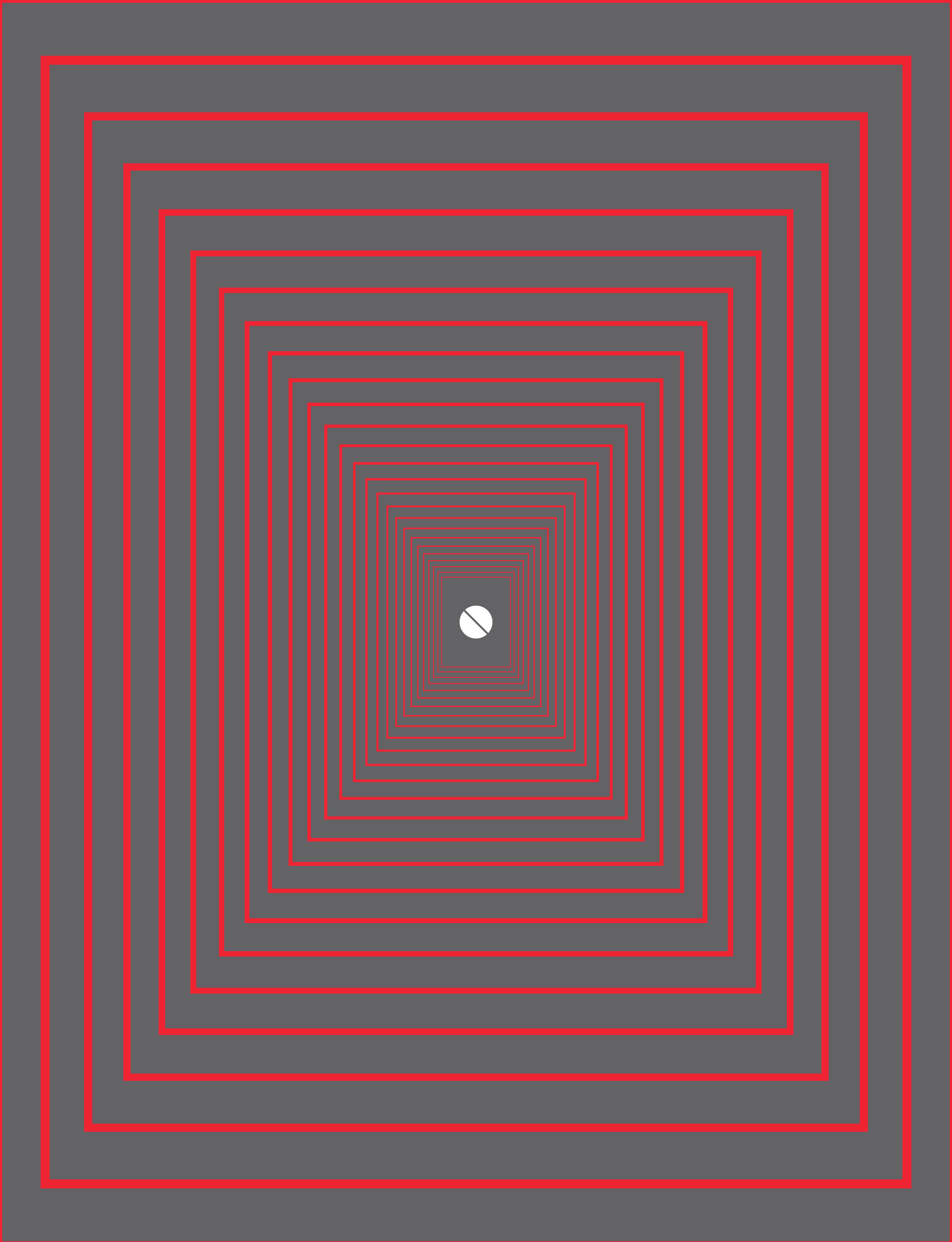
The time lines are aggressive, at least by the standards of the nuclear industry.

> The time lines are aggressive, at least by the standards of the slow-moving nuclear industry.

The Shanghai Institute aims to start up a commercial-scale solid-fuel plant by 2030 and a 100-megawatt demonstration liquid-fuel reactor by 2035. Much of the current work, Chen told me, focuses on solving the complex plumbing challenges associated with the highly corrosive molten salt. I was struck by the confidence and idealism of the young scientists working at the institute—an optimism not seen in U.S. nuclear circles since Weinberg's day.

On my last day in Shanghai, Kun Chen and I strolled around the institute's grounds. The snow was mostly gone, but the icy wind was still sharp. He showed me the campus's latest construction project: a three-story-high, warehouse-size building to house the thorium molten-salt program. All the chemistry labs, all the machine shops, all the computers, all the offices and the test loops and pumps and prototypes, will be housed here when the building opens later this year. It was just a shell at the time, but it was a symbol of China's commitment to the next nuclear era. The dream of American scientists at Oak Ridge, a half-century ago, is taking shape here, thousands of miles away.

Richard Martin, senior editor for energy at MIT Technology Review, is *the author of* SuperFuel: Thorium, the Green Energy Source for the Future.



The Quest for Better Painkillers

Researchers may soon vanquish our pain without the devastating side effects of opioids.

By Adam Piore

It happens every time James Zadina publishes a new paper or receives a write-up: the phone in his New Orleans laboratory begins to ring. The e-mails flood his inbox. The messages come from people all around the nation telling him how much they hurt.

"I get calls saying, 'I have this terrible pain. When's your medicine coming?'" Zadina says. "And my response is, 'I can't give it to you now. I'm working as fast as I can.' That's all I can say. But it's difficult."

For the last 20 years, Zadina, a researcher at the Tulane School of Medicine and the Southeast Louisiana Veterans Health Care System, has been on the front lines of a battle to defeat an ancient human adversary: physical pain. But lately his work has taken on new urgency. As opioid-related deaths and addiction in the United States reach epidemic proportions, Zadina has been attempting to engineer a new kind of painkiller that wouldn't have the devastating side effects often caused by commonly prescribed drugs such as Oxycontin.

His pursuit is difficult because the very mechanisms that make those pills good at dulling pain are the ones that too often lead to crippling addiction and drug abuse. Like their close chemical cousin heroin, prescription opioids usually cause people to become physically dependent on them. Researchers have been trying for decades to "separate the addictive properties of opiates from the pain-reducing properties," says David Thomas, an administrator at the National Institute on Drug Abuse and a founding member of the NIH Pain Consortium. "They kind of go together."

But Zadina believes he is getting close to decoupling them. Just this past winter, he and his team published a study in *Neuropharmacology* reporting that they had treated pain in rats without causing the five most common side effects associated with opioids, including increased tolerance, motor impairment, and respiratory depression, which leads to most opioid-related deaths. The next step is to test it in humans.

It's just one of a number of efforts that aim to end the long-term damage

that is being caused by relieving people of agony. Up to 8 percent of patients prescribed narcotic painkillers for chronic pain will become addicted, according to the National Institute of Drug Addiction. That's why it used to be relatively difficult for patients to obtain opioids such as codeine to treat pain, Thomas says. That began to change in the 1990s. New opioids such as Oxycontin (and new marketing campaigns by pharmaceutical companies) arrived to meet the earnest demands of pain doctors and patient advocates who argued that many people with chronic pain—which afflicts an estimated 100 million Americans—were needlessly suffering.

But the pendulum has swung so far that opioids have become the default drug even when there might be better alternatives. Dan Clauw, director of the Chronic Pain and Fatigue Research Center at the University of Michigan, says that too many doctors now are essentially telling patients, "Well, I was taught that opioids would always work in any kind of pain, and if the pain's bad enough and you're desperate enough, I'll try this class of drugs even if I am concerned about the risk of addiction."

The consequences have been devastating. In 2014, the number of deaths from opioid overdoses in the United States topped 18,000, about 50 a day—more than three times the number in 2001. And that doesn't even take into account painkiller addicts who have turned to heroin to soothe their cravings. Officials at the Centers for Disease Control and Prevention recently compared the scale of the problem to the HIV epidemic of the 1980s.

Developing any kind of better painkiller is very hard largely because pain takes complex pathways in our bodies. The signals that reach the brain and are interpreted as pain sometimes come from a problem on the periphery, or the surface, of our bodies, like when you get a cut. Other times the source of the pain signals is deeper: from damage to our nerves, which can happen with a really bad wound or, say, a back injury. And researchers such as Clauw are now finding evidence that much pain comes from a third type of situation: misfiring in the brain.

However, the presence of these different pain mechanisms also means there are a few different ways to try to solve the opioid problem. While Zadina and other scientists try to remove the dangerous properties from opioids, other new painkillers might target altogether different mechanisms in the body.

"I'm working as fast as I can," Zadina says. "That's all I can say. But it's difficult."

Make it stop

The main way to kill pain is simply to reduce the signals that the body feeds to the brain.

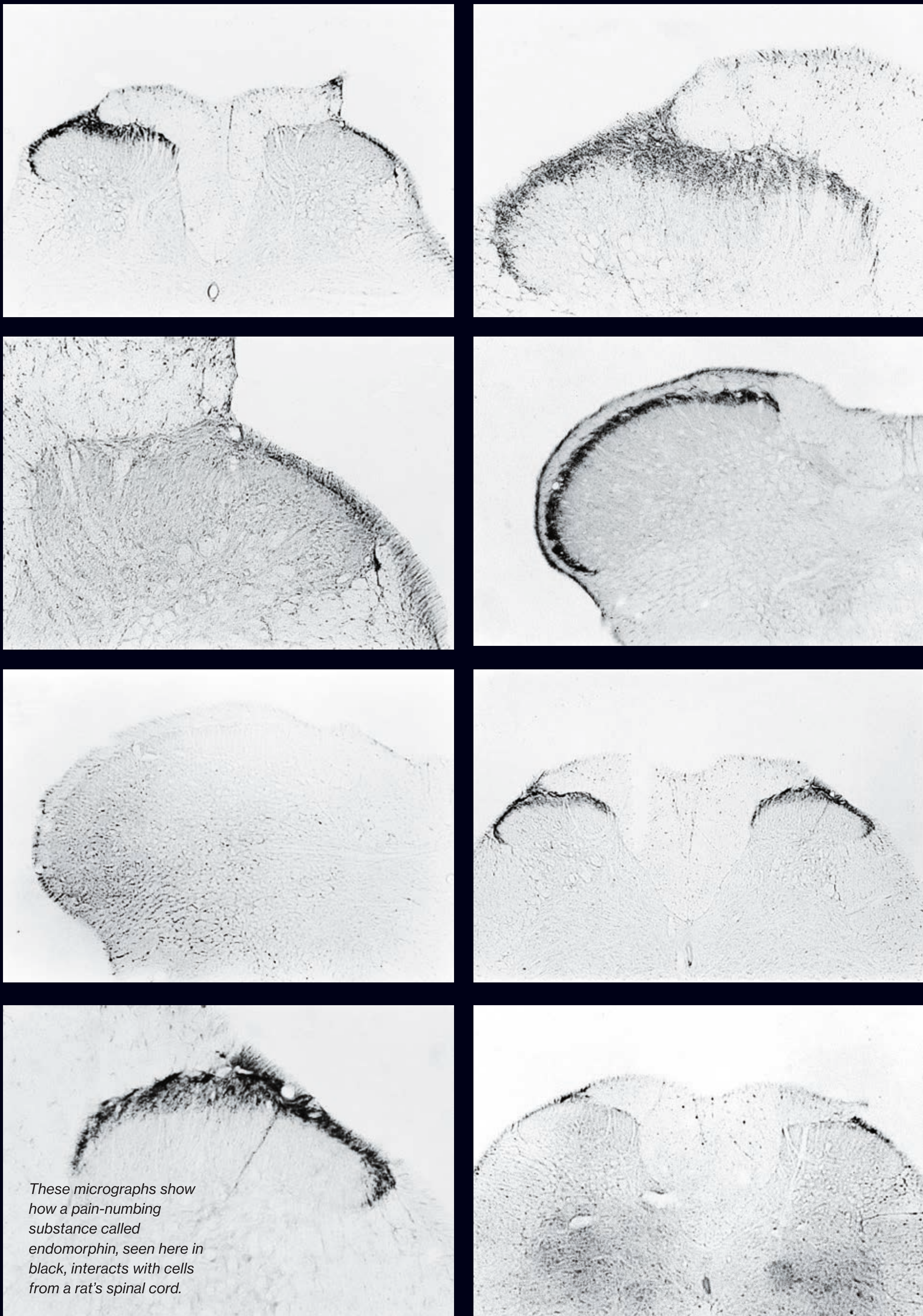
Nearly all our tissues have what are known as "nociceptive" nerve endings, tiny fibers whose job is to collect information and convey it back to the central nervous system and into the brain for processing. These fibers act as pain sensors. Some of the nerve endings respond to pressure, which causes them to send electrical impulses to the spinal cord so we actually feel hurt. Other kinds of nerve endings respond to changes in temperature, generating pain signals when things get too hot or cold. When we sustain an injury, inflammatory cells are recruited to the site and release at least a dozen different chemicals aimed at triggering other cells to come in and fight off pathogens, clean up debris, and begin rebuilding. But these inflammatory cells also cause the nerve endings at the site of the injury to fire more pain signals. In this type of localized injury, such as a sprained ankle or twisted knee, ice or anti-inflammatory drugs such as ibuprofen can be enough to tamp down the pain signals.

But sometimes—after a severe injury, an amputation, or diabetic nerve damage, for example—nerve fibers or the cells from which they originate physically change. Deep inside them, some genes can get turned on or off. That changes the number or type of active cellular machines known as sodium channels—proteins that stick out of the cells and regulate their ability to generate electrical impulses. Nerve cells talk to each other by means of these electrical impulses, and the sudden activity of extra sodium channels can cause a nerve to fire machine-gun-like bursts "spontaneously, even when there are no threatening stimuli," explains Stephen Waxman, a professor of neurology at Yale University who directs the Center for Neuroscience and Regeneration Research at a Veterans Affairs hospital in Connecticut. Those bursts leave people in extreme pain. One common cause is chemotherapy. "Sometimes that pain is so bad people say 'I can't stand it,'" Waxman says. "'I would rather die from cancer than have the pain associated with treatment.'"

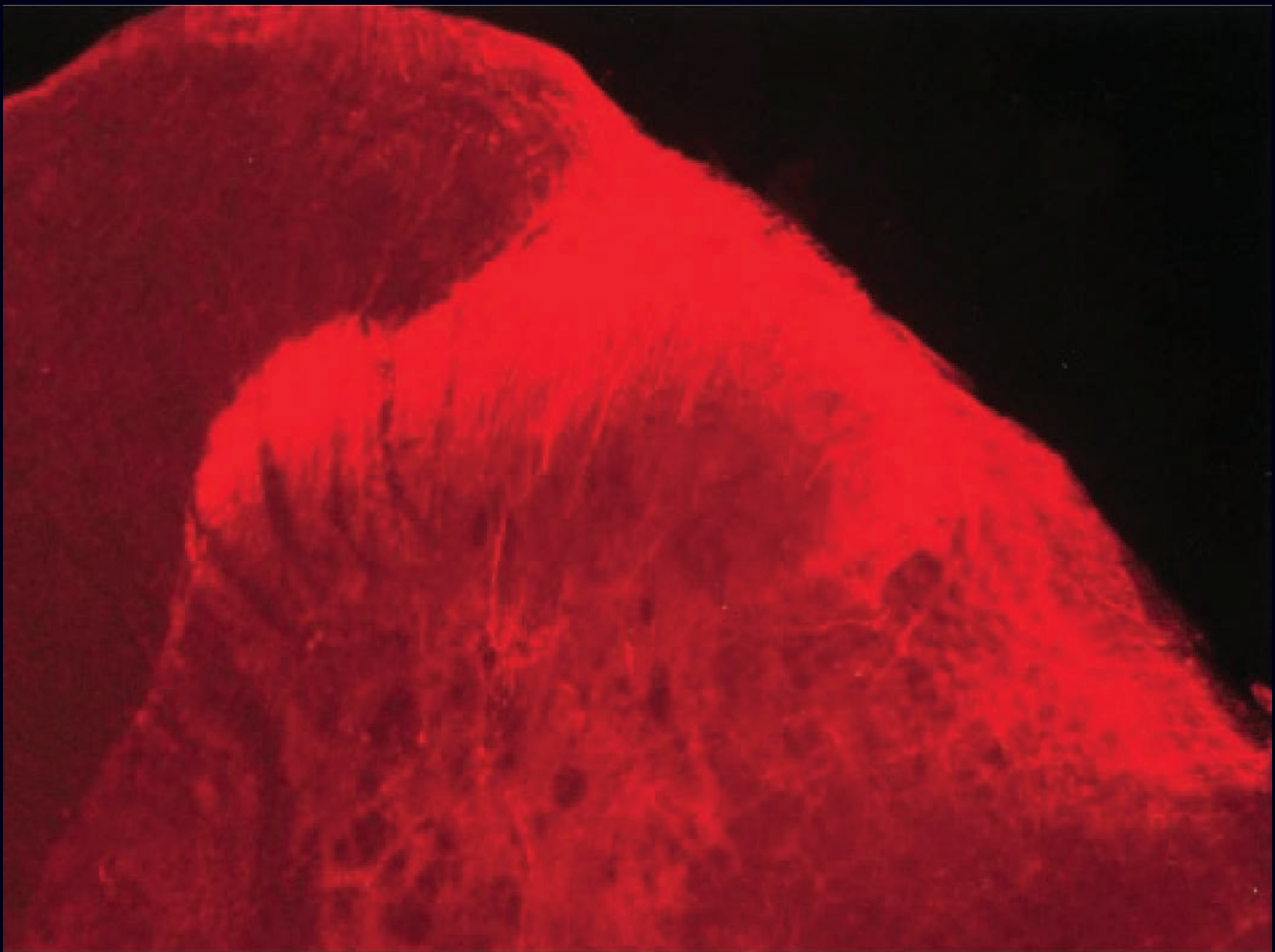
There are nine kinds of sodium channels; the numbing medicine you get in the dentist's office works by locally blunting all of them. That wouldn't work as a general pain medication, because some of these channels are present in the brain and central nervous system. But Waxman is part of a cadre of researchers hunting for ways to target just one key sodium channel. He discovered its importance by studying people who have a rare genetic mutation that prevents them from making this particular channel. Even though the channel is not found everywhere in the human body, they essentially go through life feeling no pain. Conversely, people born with a hyperactive version of it feel as though "lava has been poured into their bodies," Waxman says.

A drug developed by Pfizer, based on Waxman's discoveries, has been tested on five patients, and similar painkillers are in

COURTESY OF JAMES ZADINA



These micrographs show how a pain-numbing substance called endomorphin, seen here in black, interacts with cells from a rat's spinal cord.



An image from a 1998 paper that established the presence of endomorphin in pathways that the body uses to transmit pain to the brain.

development. Theoretically at least, these would not have major side effects.

Which brings us back to opioids.

Flipping a switch

Our peripheral nerves, where we pick up pain signals, lead back to the spinal column, where they connect with nerve cells that carry messages into the central nervous system and to neurons in the brain, at which point we feel the pain.

This is where all opioids, from Oxycontin to heroin and morphine, work their magic. They do so by binding to what are known as mu receptors at the junctions where nerve cells meet. That essentially flips a switch that reduces the ability of these cells to fire. So when nerve fibers at the periphery of the body send pain signals up to the brain for processing, the neurons that would normally make us feel this pain don't respond.

"Opioids don't touch the pain source; they only turn off the appreciation of the pain in the brain," says Lewis Nelson, a professor of emergency medicine at New York University School of Medicine, who sat on a panel that recently recommended opioid guidelines for the Centers for Disease Control. "A small dose of an opioid just changes the sensation from being something that is quite irritating to being something that you don't seem to care about as much."

Mu receptors respond not only to painkilling drugs but also to "endogenous opioids," natural signaling agents produced by our bodies—like the endorphins that are released during exercise, producing the so-called "runner's high." The problem is that the body doesn't seem to respond to drugs such as heroin and Oxycontin in the same way it does to the endogenous substances.

Unlike endogenous opioids, pain drugs often activate specialized cells in the central nervous system, known as glia. Glia clean up cellular debris in the body and help regulate the response to injuries to the central nervous system. But when activated, they produce inflammatory substances—which can cause the body to register *more* pain signals. Many researchers, in fact, believe this increased activation of glial cells may be what causes the dangerous buildup of tolerance that makes opioids less effective over time, so that a patient needs higher doses to feel their effects. Eventually those higher doses can cause deadly respiratory problems.

All this might be avoided if Zadina can finally develop a synthetic opioid more like the body's own substances—one that hits the mu receptors without activating glial cells. In the 1990s, he and his team isolated a previously undiscovered neurochemical in the brain, a pain-numbing substance they named endomorphin. He has been attempting ever since to perfect synthetic versions of it.

One of those versions was the drug that Zadina tested on rats in the study reported this past winter in *Neuropharmacology*. Like some of his previous compounds, this version appeared to be as good as or possibly better than morphine at relieving the animals' pain without causing the worst side effects. Now he is in talks with several investors and biotech companies interested in turning it into a pill for people. Once he and his collaborators raise the money to start their own company, or ink a deal with a licensing partner, they intend to seek approval for early-stage human trials. "You never know until you actually put it in humans," he says.

Zadina's drug would still be likely to activate the reward areas of the brain, and it might generate a mild high that could predispose some to addiction. But the rapid escalation of tolerance that opioids normally cause—and the physical withdrawal symptoms people endure when they stop taking them—would probably be removed from the equation. "I want to take away the dilemma that both patients and physicians face, of 'Do I treat this pain adequately and risk addiction or do I treat the pain inadequately because I don't want to use opioids?'" Zadina says. "That's what drives me."

But even if his new drug succeeds, neither it nor new sodium-channel painkillers are likely to treat a type of pain we weren't even sure existed until recently—pain that does not seem to respond at all to opioids. Michigan's Clauw has been studying this kind of pain for the past 20 years. From brain imaging studies, he has determined that it is caused by misfiring in the brain rather than a problem at the site where the pain seems to be coming from. He contends that this is the most common reason for pain in younger people suffering from conditions that have long confounded doctors, including fibromyalgia, certain headaches, and irritable bowel syndrome. What should those patients take instead of the opioids they are often prescribed? Many of them, Clauw argues, should be on drugs that can actually halt the misfiring by boosting neurotransmitters. Some drugs originally developed as antidepressants achieve this.

The NIH's Thomas points to Clauw's research as evidence that opioids today are simply overprescribed.

"If you get in a car accident, get wounded in battle, your arm gets blown up or something, and you're in really severe pain, they will knock out severe pain pretty darn quickly," says Thomas. "But right now they're being used for all sorts of other cases where they're probably not beneficial to the patient in the long run."

> Some of Zadina's experimental compounds have given rats as much pain relief as morphine.

Adam Piore is the author of The Body Builders: Inside the Science of the Engineered Human, *which will be published in February.*

COURTESY OF JAMES ZADINA

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35 Innovators under 35

The people in our 16th annual celebration of young innovators are disrupters and dreamers. They're inquisitive and persistent, inspired and inspiring. No matter whether they're pursuing medical breakthroughs, refashioning energy technologies, making computers more useful, or engineering cooler electronic devices—and regardless of whether they are heading startups, working in big companies, or doing research in academic labs—they all are poised to be leaders in their fields.

Hundreds of people were nominated for this group. After *MIT Technology Review*'s editors narrowed the list, outside judges evaluated the quality and potential impact of the finalists' work, guiding the selections you'll find here.

Judges

Polina Anikeeva
Assistant Professor of Materials Science and Engineering, MIT

Zhenan Bao
Professor of Chemical Engineering, Stanford University

Emily Cole
Chief Science Officer, Liquid Light

David Berry
General Partner, Flagship Ventures

Edward Boyden
Co-director, MIT Center for Neurobiological Engineering

Yet-Ming Chiang
Professor of Materials Science and Engineering, MIT

James Collins
Professor of Medical Engineering and Science, MIT

John Dabiri
Professor of Civil & Environmental Engineering and Mechanical Engineering, Stanford University

David Fattal
CEO, Leia

Tanuja Ganu
Cofounder, DataGlen

Javier García-Martínez
Director, Molecular Nanotechnology Laboratory, University of Alicante, Spain

Julia Greer
Professor of Materials Science and Mechanics, Caltech

Christine Hendon
Assistant Professor of Electrical Engineering, Columbia University

Eric Horvitz
Managing Director, Microsoft Research

Rana el Kaliouby
CEO, Affectiva

Jennifer Lewis
Professor of Biologically Inspired Engineering, Harvard University

Hao Li
CEO, Pinscreen; Assistant Professor of Computer Science, University of Southern California

Carmichael Roberts
Entrepreneur and General Partner, North Bridge Venture Partners

John Rogers
Professor of Chemistry and Materials Science & Engineering, University of Illinois

Umar Saif
Vice Chancellor, Information Technology University, Punjab

Rachel Sheinbein
Managing Director, Makeda Capital

Leila Takayama
Acting Associate Professor of Psychology, UC Santa Cruz

Jennifer West
Professor of Engineering, Duke University

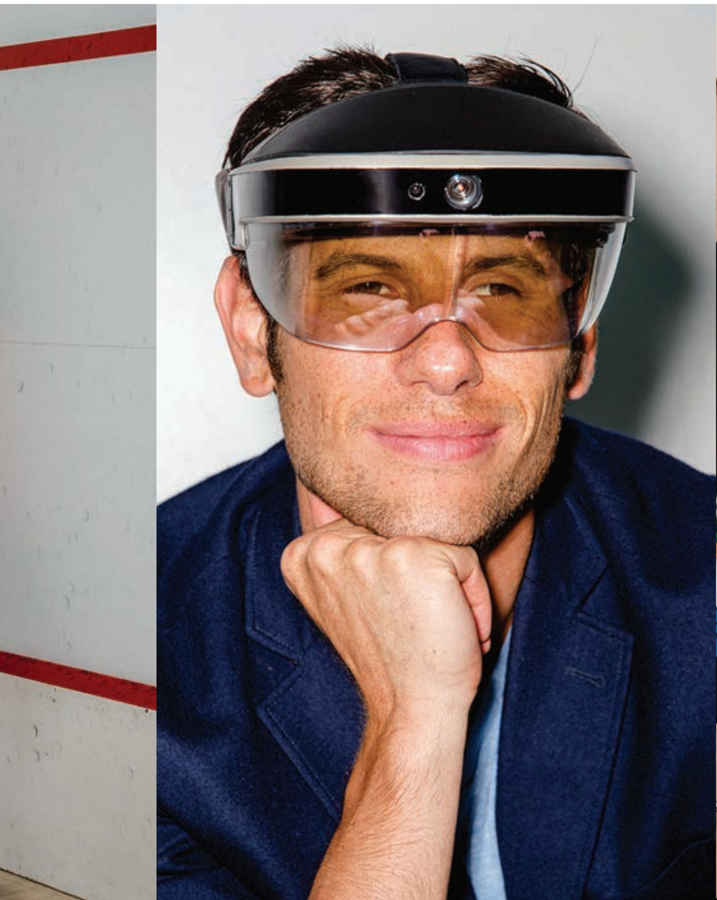
Jackie Yi-Ru Ying
Executive Director, Institute of Bioengineering and Nanotechnology, Singapore

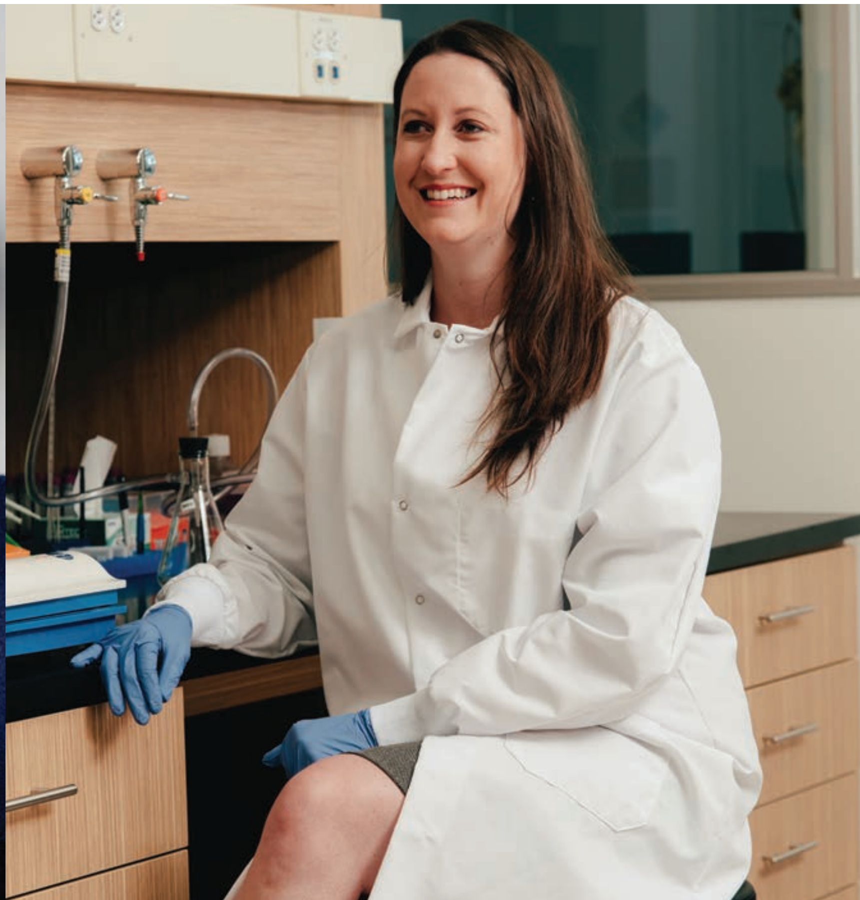
Ben Zhao
Professor of Computer Science, UC Santa Barbara

Daphne Zohar
CEO, PureTech

NEXT YEAR Suggest candidates for the 2017 list at technologyreview.com/nominate

JUSTIN TSUCALAS, RC RIVERA, DAMIEN MALONEY, DAMIEN MALONEY, TIMOTHY O'CONNELL





Visionaries

By looking at things a bit differently from everyone else, they find powerful new uses of technology.

Featuring

Jean Yang / Evan Spiegel / Nora Ayanian / Maithilee Kunda / Kevin Esvelt / Jonathan Downey

Jean Yang

Carnegie Mellon University

Why don't computers keep our personal data secure by default?

When programmers create a feature for an app or a website, even something as simple as a calendar, they should code in protections so the personal information that the feature needs to access—such as your location—doesn't slip out onto the Internet. Needless to say, they sometimes fail, leaving our data to be exploited by hackers. "Just like there are many ways to sink a boat," says Jean Yang, "there are many ways to leak information."

That's why Yang created Jeeves, a programming language with privacy baked in. With Jeeves, developers don't necessarily have to scrub personal information from their features, because Yang's code essentially does it automatically. "It is a double hull for information leaks," Yang says.

"Just like there are many ways to sink a boat, there are many ways to leak information."

She has uploaded the code to open-source libraries for anyone to use. And this fall she begins as an assistant professor of computer science at Carnegie Mellon, where she can try to get her ideas to spread further. "Giving people tools to create technology is incredibly empowering," she says. —*Patrick Doyle*

Evan Spiegel

Snapchat

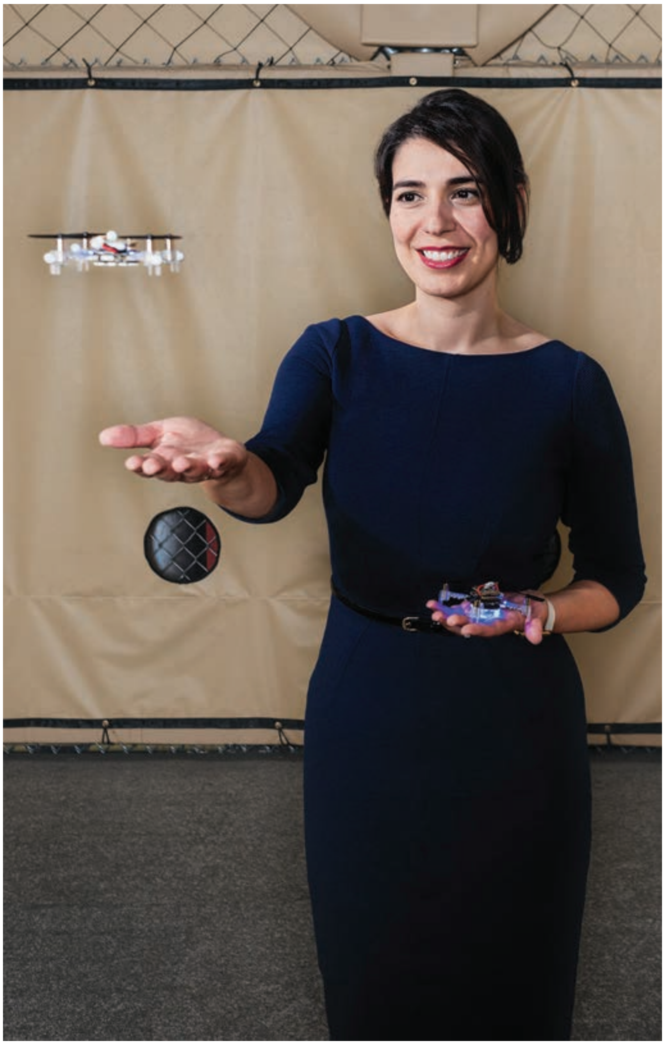
The cofounder of Snapchat figured out that people wanted something different from social media.

LEONARD GRECO; STEVE JENNINGS/GETTY

At the center of Snapchat—the disappearing-photo social network valued at $20 billion, used by 150 million people—sits an exotic-car-driving, engaged-to-a-supermodel 26-year-old genius. Or jerk. Or both—it's hard to tell. Evan Spiegel is kind of a recluse. The guy behind this new media empire follows only about 50 people on the mobile app he helped create. (One of them is the magician David Blaine.) He declined to speak to me, which is fitting, because what Snapchat is, what Spiegel understands better than anyone, might be the opposite of an interview with a magazine.

Snapchat is often compared to Facebook, and Spiegel to Mark Zuckerberg. Which makes sense, especially since Facebook tried to buy Snapchat for $3 billion before releasing its own knockoff versions that promptly fell into irrelevance. And both founders are college dropouts (Spiegel from Stanford, Zuckerberg from Harvard). But Facebook is a company built on making your personal data public and delivering targeted ads; the whole point of Snapchat is to delete your images or videos after you send them to your friends. Snapchat, Spiegel has said, is based on the idea that "ephemeral should be the default."

In its six years of existence—an epoch in startup time—the company has outlasted rivals like Poke and Ansa and Gryphn and Vidburn and Clipchat and Efemr (I swear I'm not making these up) and Wink and Blink and Frankly and (I promise you) Burn Note and Glimpse and Wickr. It reaches 41 percent of U.S. 18- to 34-year-olds *every day* and generates revenue from media companies and advertisers that publish snaps in dedicated channels. What did Snapchat do right that others didn't? One thing you immediately notice upon downloading the app is how much it requires of you. You can't just sit back and watch—you, too, must snap. The home screen practically begs you to take a picture or shoot a video. Photography once was all about capturing a moment forever; Spiegel's great insight was that now the best way to make people pay attention is to capture that moment, share it, and watch as it disappears. —*Ryan Bradley*



Nora Ayanian

University of Southern California

To build better machines, a roboticist goes far outside her field for guidance.

Nora Ayanian calls robots people. It's not some weird affectation; it helps her with her work.

She's a computer scientist who thinks machines should work together to get things done. Let's say a farmer wants to have drones autonomously survey crops and take soil samples. You couldn't program each drone with the same set of commands, because each would have a different task and would have to solve different problems as it navigated. You know what is good at solving problems on the fly, in a group that draws on various skills from different individuals? People.

So Ayanian studies robot coördination by studying people. One way is by having groups of humans play a simple video game that limits their senses and stifles communication. They need to figure out how to do "something meaningful" together, as she puts it, such as arranging their on-screen figures into a circle. Ayanian watches how people coöperate on such tasks with as little information as possible.

Distributed and diverse teams are always better at problem-solving.

Why not just create a dictator robot—one machine that sees the whole field and directs other drones? Well, Ayanian counters, what happens when the dictator robot runs out of power? Or crashes? Distributed and diverse teams, she says, are always better at problem-solving, once they learn to work together.

—Ryan Bradley

Maithilee Kunda

Vanderbilt University

People on the autism spectrum are inspiring her novel approach to creating artificial intelligence.

"My research began in graduate school when I was working on artificial-intelligence systems and read *Thinking in Pictures* by Temple Grandin, a professor of animal science who talks about how her autism gives her this unique visual way of thinking compared to most people.

"I thought: That's interesting. Most AI systems are not 'visual thinkers' like her. Most AI systems use variables, numbers, lists, and so on, and they reason using mathematical and logical operations. These systems are 'verbal thinkers.' What if you had an AI system that used data made up entirely of images and reasoned only using visual operations, like rotating images around or combining images together? If Temple Grandin can do amazing things because of her visual thinking abilities, it seemed to me that the same should be true of AI systems.

"I've been taking what we learn from people on the autism spectrum who have interesting visual abilities and building that into AI systems. It's early, but I expect that they ultimately will be very valuable. If we want to help students learn to solve difficult problems, then we ought to have several AI tutors that can show students different ways of solving the same problem. If we want to help doctors find patterns of disease outbreaks, then we ought to have multiple AI analysts that can sift through the data using different styles of pattern finding."

—as told to David Talbot

DAMON CASAREZ; COURTESY OF MAITHILEE KUNDA; LEONARD GRECO

Kevin Esvelt

MIT

A scientist who is developing new gene-editing techniques also warns of their potential.

His Job
Works at MIT's Media Lab to develop ways of influencing how ecosystems evolve.

The Back Story
Visited the Galápagos Islands at age 10. "I knew evolution would impact what I wanted to do."

His Burning Issue
Gene drives, a new technology that could be used to quickly spread traits among wild creatures such as mosquitoes.

What's at Stake
Wiping out mosquitoes, and maybe malaria. "Unimaginable amounts of suffering occur in the wild, and evolution doesn't care," he says.

The Dilemma
Are gene drives safe enough to ever use in the open, or will they have dangerous unintended consequences?

Esvelt's Take
No gene drive able to spread globally should be released, he argues. Or even tested. Scientists need to disclose their plans.

His Solution
He's designed safer gene drives that can be controlled.

The Reviews
Raising awareness about the potential threats of gene drives is "a home run for biosecurity," says the FBI.

Hobbies
Risky ones. Unicycling and hang-gliding.

—Antonio Regalado

Jonathan Downey

Airware

The creator of control software for drones has foreseen the advantages of autonomous aircraft for years.

2002–2006 As an engineering and computer science student at MIT, Downey starts a group that builds drones and competes against other colleges.

2005–2010 While working for Boeing, he develops flight-control software for an autonomous helicopter funded by the Pentagon.

2011 Founds a startup called Airware out of frustration with what he calls "inflexible and costly" autopilot systems for unmanned aircraft that made it hard to add new capabilities. Also spends five months flying tourists in a turboprop plane between Las Vegas and the Grand Canyon.

2012 Airware ships its first control software to drone manufacturers.

2014 General Electric invests in Airware, saying drones could help make it safer and cheaper to maintain industrial equipment such as power lines.

2015 Airware launches several products intended to help big companies use drones. For instance, software designed by former game developers lets companies take aerial photos of sprawling facilities as easily as you would click on a map. State Farm uses Airware's technology to inspect roofs after weather damage.

2016 U.S. regulators remove rules that had tightly limited what companies could do with drones, clearing a path for many more companies to use Airware's services.

2025 An industry group, the Association for Unmanned Vehicle Systems, predicts commercial drones will have created $80 billion in business value and 100,000 jobs by this time. "We will not be able to imagine doing our jobs without them," says Downey.

—Tom Simonite

Airware has raised more than $70 million in venture capital to make it easy for companies to do things with drones.

DAMIEN MALONEY

CRIME FORECASTING CHALLENGE

INNOVATIONS IN FORECASTING HAVE THE POWER TO MAKE COMMUNITIES SAFER.

We're looking for the brightest minds in data science to advance place-based crime forecasting through the use of open crime data. Are you up for the challenge? Enter your forecasts for a chance to win prizes totaling $1.2 MILLION.

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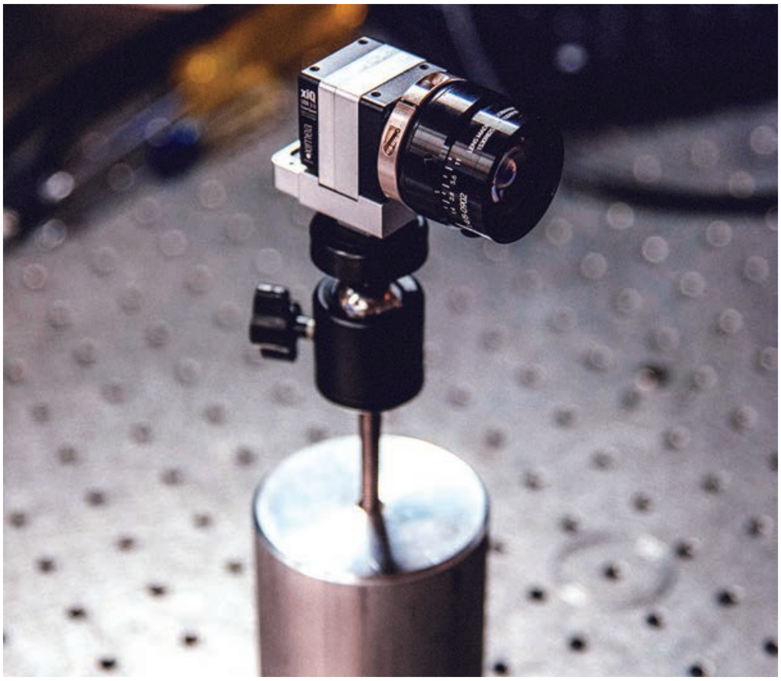
Inventors

These innovators are building the stuff of the future, from a smart sweatband to tomorrow's memory technology.

Featuring

Alex Hegyi / Evan Macosko / Wei Gao / Muyinatu Lediju Bell / Adam Bry / Kendra Kuhl / Desmond Loke / Jiawei Gu / Dinesh Bharadia



Hegyi's prototype is a modified USB camera. Software lets him look at images in a new light, revealing novel details.

Alex Hegyi

PARC

A new type of camera could let smartphones find counterfeit drugs or spot the ripest peach.

No matter how good your smartphone camera is, it can show you only a fraction of the detail Alex Hegyi can with the one he's built at Xerox's PARC in Palo Alto, California. That's because Hegyi's camera also records parts of the spectrum of light that you can't see.

Since Hegyi's camera logs a wider range of wavelengths, it can be used for everything from checking produce at the grocery store (fruits increasingly absorb certain wavelengths as they ripen) to spotting counterfeit drugs (the real ones reflect a distinctive pattern). In the near future, Hegyi hopes, his technology can be added to smartphone cameras, so anyone can make and use apps that harness so-called hyperspectral imaging.

Such systems have been around for years, but they have been big and expensive, limiting them to non-consumer applications like surveillance and quality control for food and drugs. His version, which is much simpler and more compact, relies on a black-and-white USB camera. He adds a liquid crystal cell, set between polarizing filters, in front of its image sensor. He also created software, which he runs on a connected tablet computer, to process the images.

Three to five years from now, Hegyi thinks, your phone could be revealing information that isn't available in the visible spectrum of light. With such a tool, he says, "consumers themselves don't have to know anything about wavelengths—they can take a picture and the display can say 'counterfeit' or 'real.'" Or it might say the peach is ripe. —*Rachel Metz*

DAMIEN MALONEY

Hegyi's camera records parts of the spectrum that you can't see.

Evan Macosko

Harvard Medical School

A breakthrough in probing how cells create complex tissues and organs.

Problem

To truly understand the human genome, we need better insight into how individual cells differ. While every cell in a person's body has basically the same DNA blueprint, there's great variation in the way that genetic information is actually acted on, or expressed, at any given time. It's the reason one cell becomes a neuron that plays a role in memory, while another cell becomes part of a person's toenail. Even a given organ, like the brain, encompasses different types of cells, and individual cell types, too, have variations. Inadequate knowledge about how genes are expressed in different cells is greatly hampering progress in genomic medicine.

Solution

Evan Macosko has helped invent a technology called Drop-Seq, which allows a researcher to look at thousands of cells, one by one, to determine how each is carrying out its genetic instructions. Such analysis of a single cell can be done with existing tools, but it is typically painstaking, expensive work that involves dropping individual cells into tiny wells. "If you get two cells in a well, you're screwed," says Macosko.

To greatly speed up the process, Macosko figured out how to take each cell he wanted to analyze, break it apart, and attach the expressed genes to a tiny bar-coded bead. Once material from each cell is labeled, the genes can be analyzed rapidly—all for a cost of just seven cents a cell.

Macosko says he and his team have nearly finished profiling hundreds of thousands of cells spanning most of the mouse brain. Next stop: the 86 billion neurons and innumerable other cells that make up the human brain. By analyzing the great variation in the cells in our brains, he hopes to identify the rogue cells that are malfunctioning or interfering with normal function in disorders like schizophrenia, autism, and Alzheimer's.

—Michael Reilly

Wei Gao

University of California, Berkeley

The engineer has built sweatbands that monitor your health.

"I grew up in a small village in Xuzhou, China. When I was a child I saw a lot of people around me dying of different diseases. Many people don't realize there's a problem until it's too late. I thought, in the future I should design a wearable electronic device to monitor health and tell us what's going on and what's going wrong before it gets bad.

"Our body is generating data all the time. There are so many wearable devices now—the Apple watch, the Fitbit—but they mainly track physical activities or vital signs. They can't provide information at the molecular level.

"It came into my mind: what about sweat?"

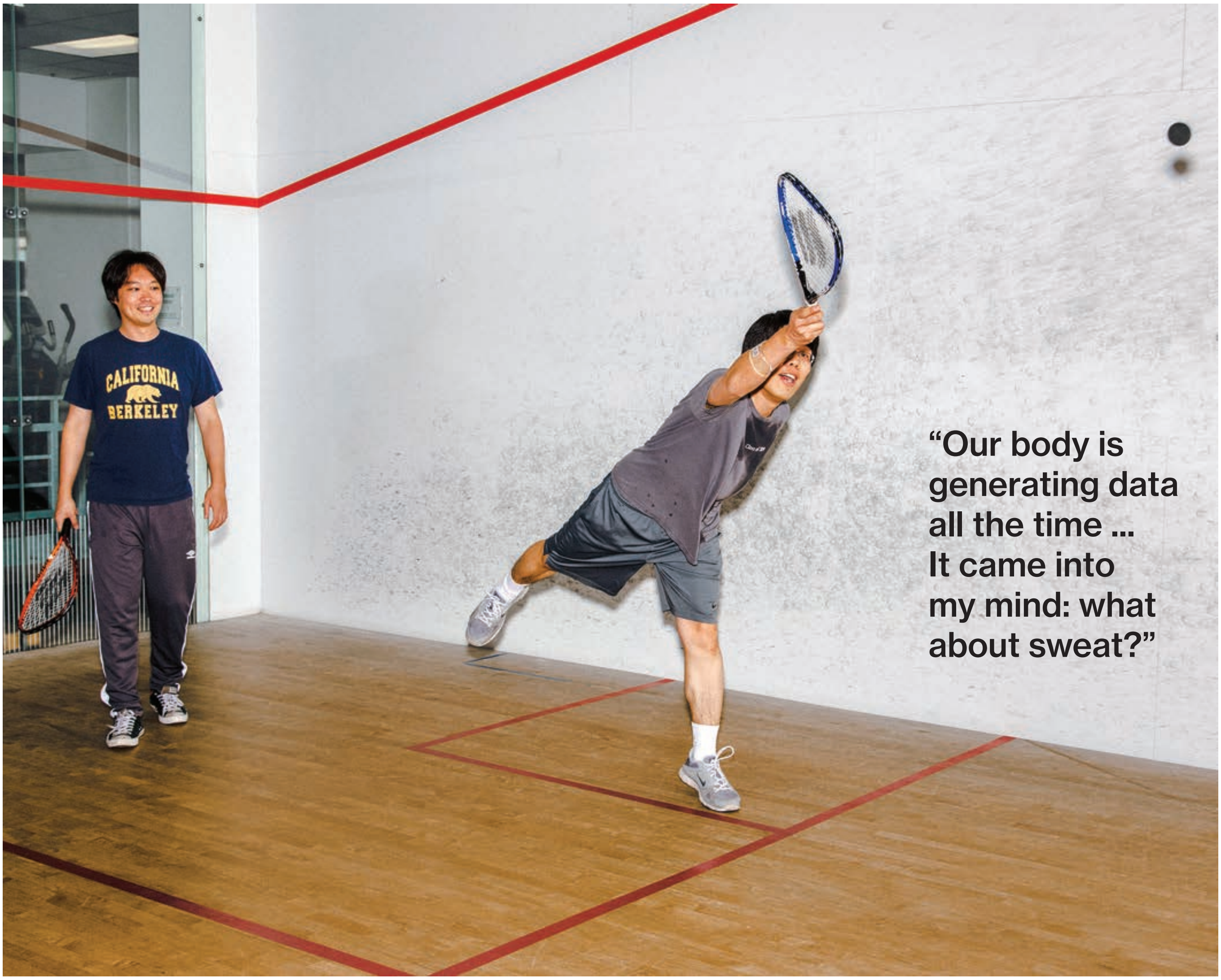
This year, Gao made a sweatband that combines sensors with electronic processors and a Bluetooth transmitter on a flexible printed circuit board. If you wear the band, it wirelessly transmits data about what's in your sweat to a cell phone running an app.

Gao's device has sensors that interact with chemicals including glucose and lactate, causing a detectable change in their electrical current. Other sensors change their voltage in response to sodium or potassium. A recent addition includes sensors that can pick up on toxic heavy metals excreted in the sweat.

The challenge now is to figure out whether and how these measurements correspond to meaningful changes in health. So Gao is working with exercise physiologists on clinical studies to look for correlations that will help spot signs of trouble before it's too late.

—Katherine Bourzac

LEONARD GRECO



"Our body is generating data all the time ... It came into my mind: what about sweat?"

Gao wears his sweatband that uses sensors on a flexible circuit board.

DAMIEN MALONEY

Her imaging solution could particularly help people who are obese, because fat tissue can distort ultrasound waves.

JUSTIN TSUCALAS

Muyinatu Lediju Bell

Johns Hopkins University

Creating clearer imaging to spot cancer earlier and more accurately.

When biomedical engineer Muyinatu Lediju Bell was an undergraduate at MIT, her mother died of breast cancer. Bell thought her mother might have survived if she had been diagnosed sooner, so she decided to investigate what makes some ultrasound images blurry, a problem that limits a doctor's ability to screen for and diagnose cancer and other diseases.

As a doctoral candidate at Duke University, Bell developed and patented a novel signal processing technique that produces clearer ultrasound images in real time. The solution could particularly help diagnose problems in people who are obese, because fat tissue can scatter and distort ultrasound waves, delaying the detection of a serious disease. "I think it's unfair that a longstanding technology does not serve a huge group of people that should be able to benefit from it," she says.

Beyond ultrasound, Bell is now working to improve another type of noninvasive medical imaging technique. Called photoacoustic imaging, it uses a combination of light and sound to produce images of tissues in the body. She is especially interested in using it for real-time visualization of blood vessels during neurosurgeries to lower the risk of accidental harm to the carotid artery, which supplies blood to the brain. Her lab at Johns Hopkins plans to launch a pilot study of the technology in patients in 2017. *—Emily Mullin*

"At the company I cofounded, Skydio, we looked at all the things people wanted to do with drones and realized that the products are primitive compared to what's possible. Today the typical consumer experience is you take it out of the box and run it into a tree.

"We're building a drone for consumers that understands the physical world, reacts to you intelligently, and can use that information to make decisions. It has cameras positioned in a way so that computer vision can track its motion and understand the 3-D structure of the world. It also understands 'This is a person,' 'This is a tree.' We've demonstrated the ability to fly autonomously in close proximity to obstacles such as trees safely and reliably, and to follow someone walking, running, or cycling.

"On a week-to-week basis you can see the thing getting smarter and being capable of more. It shows up in the way it behaves and responds in different situations.

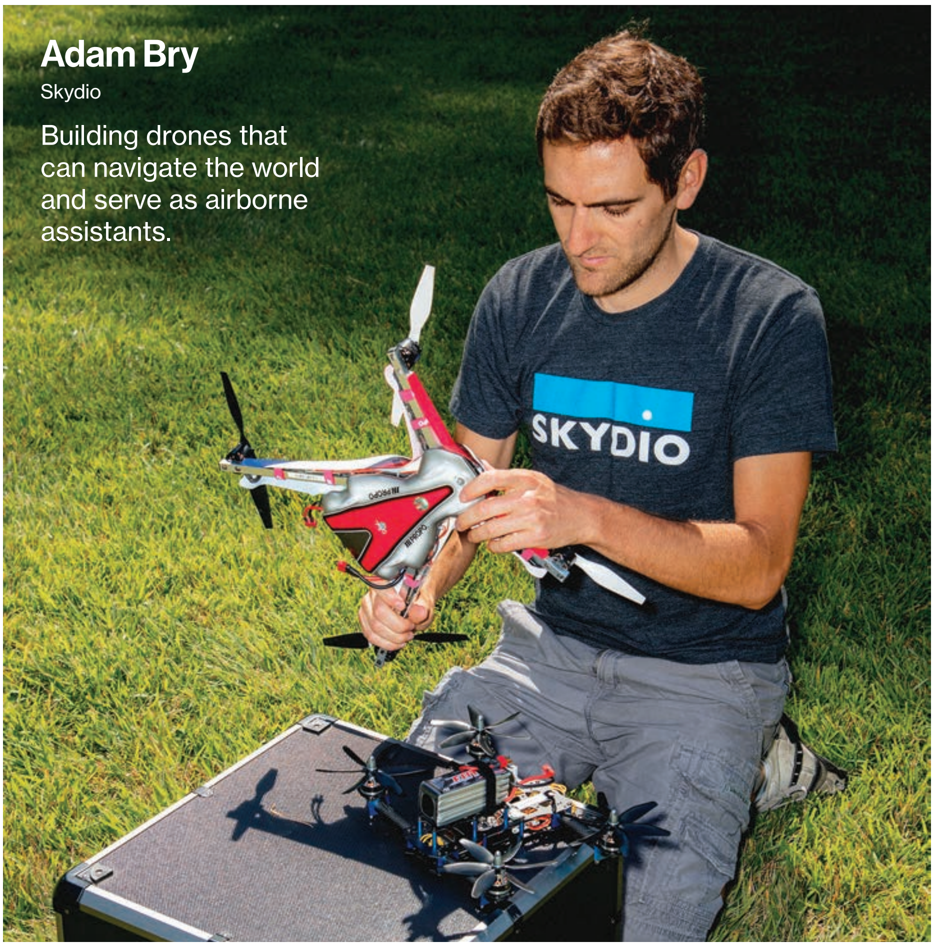
"We aren't saying a lot about our product yet, but it'll be a high-end consumer device smart enough to fly itself as well as or better than an expert pilot. Devices that understand the world and can respond to you and take actions will open up things that don't exist today. A flying camera that can be anywhere around you would be a very powerful thing. Drones are likely to be the first widely deployed category of mobile robot. As they start to get out into the world and people start to interact with them, it's going to lead to some interesting places."

—as told to Tom Simonite

Adam Bry

Skydio

Building drones that can navigate the world and serve as airborne assistants.



DAMIEN MALONEY

Kendra Kuhl

Opus 12

She developed a simple reactor to turn carbon dioxide into useful chemicals.

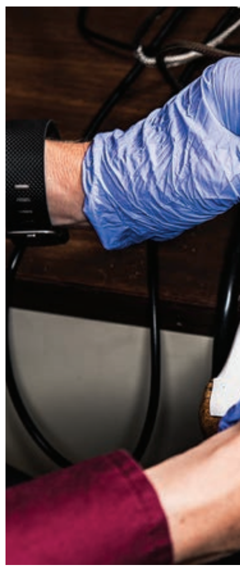
Growing up in rural Montana, Kendra Kuhl watched the namesake ice formations of nearby Glacier National Park shrink. “We could see global warming happening,” she says. The sight drove her professional ambitions. “I liked the idea of putting atoms together in new ways that are potentially friendly to the environment,” she says.

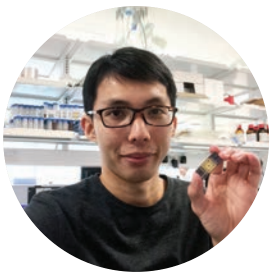
That’s just what Kuhl hopes to do through the startup she cofounded in 2014. Opus 12 is working on a reactor that will take the carbon dioxide emitted by power plants and make useful chemicals from it.

At Cyclotron Road, a startup incubator at the Lawrence Berkeley National Laboratory, Kuhl shows off one of Opus 12’s prototypes, a small reactor with an input for carbon dioxide and an output spigot connected to an instrument that analyzes the products. The key to the technology is the design of the reactor, which incorporates a family of catalysts she collaborated on during her graduate work at Stanford University. Sandwiched inside the metal reactor chamber is an electrode that uses a membrane coated with the catalysts. They enable the carbon reactions to occur at low temperature and pressure, without requiring large amounts of energy.

Opus 12 is not the first company to work on converting carbon dioxide into widely used chemicals. But its improved catalysts and scalable reactor design set the company apart, says Kuhl. Still, the company has far to go before it can begin competing with traditional chemical suppliers. By the end of 2017, Opus 12 plans to build a reactor with a stack of electrodes that can produce several kilograms of product a day. *—Katherine Bourzac*

Kendra Kuhl’s reactor uses novel catalytic nanoparticles (black square in the bottom photos). The reactor (bottom, far right) has inputs for carbon dioxide and outputs for the chemicals.





Desmond Loke

Singapore University of Technology and Design

Throw away your RAM and flash drive. Here’s a better type of memory.

Computer designers have long desired a universal memory technology to replace the combination of RAM—which is fast but expensive and volatile, meaning it requires a power supply to retain stored information—and flash, which is nonvolatile but relatively slow.

The urgency is increasing as Moore’s Law, which for so long governed the blistering pace at which silicon transistors shrank, begins to peter out. If we can’t fit many more transistors on a RAM chip, we need to find a fast, cheap new nonvolatile memory technology that can store vast amounts of data.

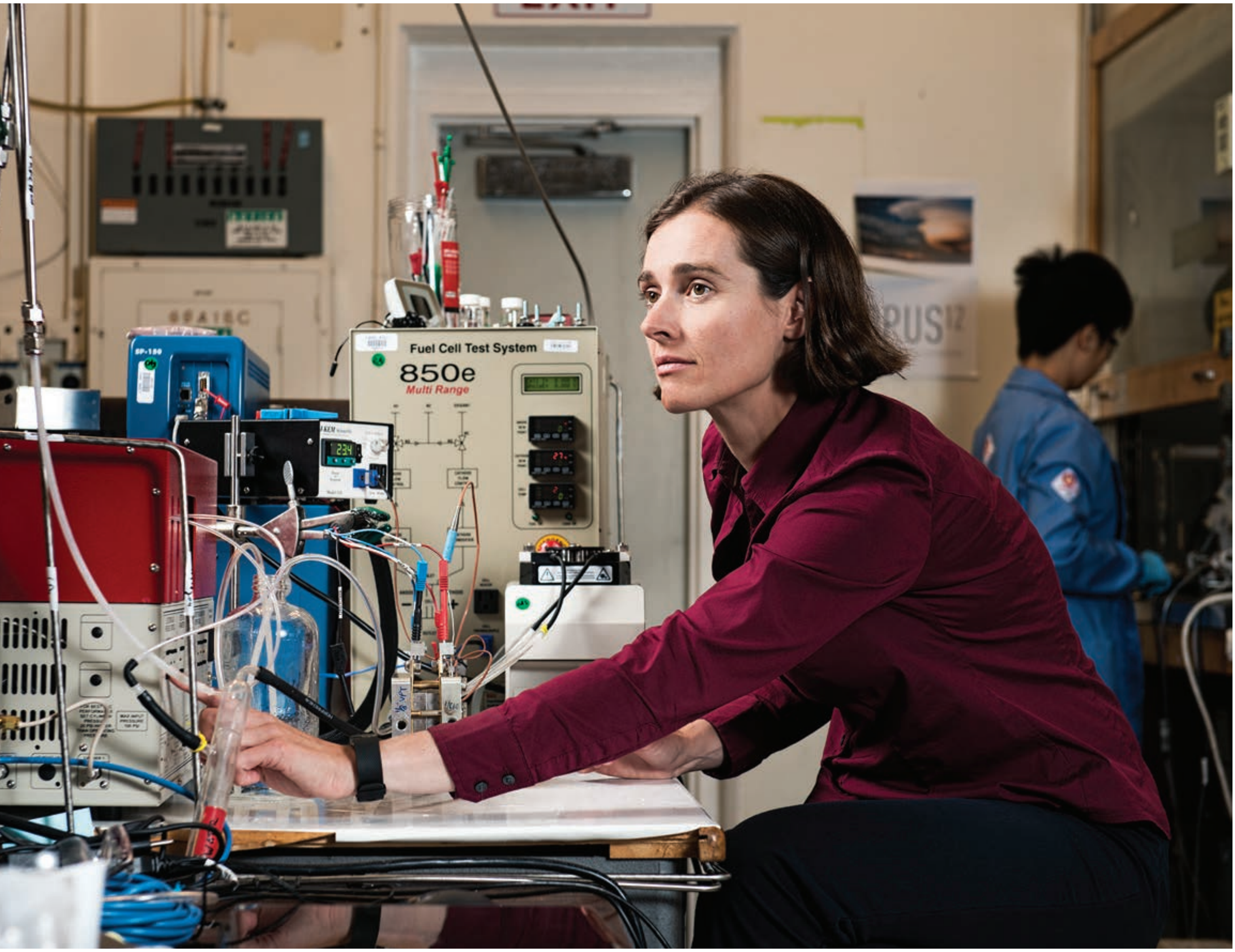
One promising alternative to the combination of RAM and flash is phase-change materials. This new type of memory stores data not by turning electric current on and off in transistors but by switching a type of material called chalcogenide glass between amorphous and crystalline states. Potentially, it is fast like RAM and nonvolatile like flash. Since 2010, Desmond Loke and his colleagues have solved several critical problems holding up its commercialization.

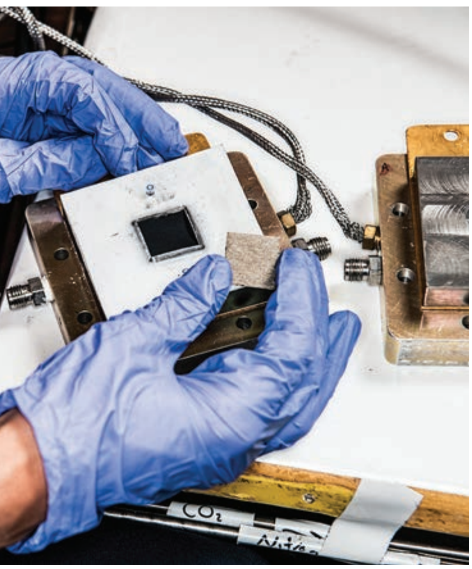
As a result of the advances, the Singapore researcher has now created a version of phase-change memory that is as fast as RAM chips and packs in many times more storage capacity than flash drives.

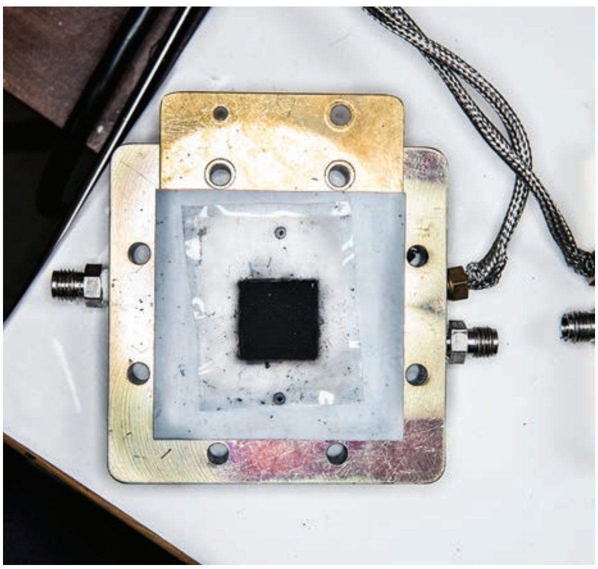
For years, researchers have been unable to get the speed at which a material changes from an orderly crystal to amorphous glass—the *1* and *0* states—any faster than about 50 nanoseconds, whereas RAM chips take less than a nanosecond to switch transistors on or off. But by applying a small, constant charge to the material, Loke found he could reduce switching time to half a nanosecond. He and his coworkers also reduced the size of a memory-cell bit to just a few nanometers. And he figured out how to vastly reduce power consumption and allow cells to be stacked in three dimensions to pack in even more memory capacity.

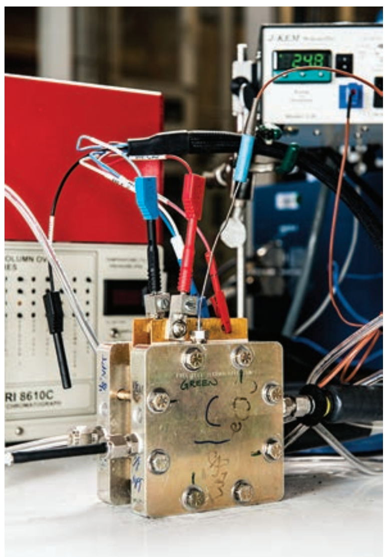
—Michael Reilly

WINNI WINTERMEYER; COURTESY OF DESMOND LOKE


Fuel Cell Test System
850e
Multi Range



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Jiawei Gu

Baidu

The AI expert designs interfaces that let technology assist rather than annoy.

When we meet at a café in Beijing's 798 Art District, a creative hub in China's capital, Jiawei Gu has turned off the notification pings from Tencent's WeChat, China's ubiquitous messaging app, on his smartphone. When he glances quickly to check the screen, he has "more than 17,000 unread messages." The way we interact with information technology is broken, he says. "I don't want to be captive for checking buzzes," Gu says.

Gu is Baidu's go-to engineer for designing better models of "human-computer interaction." One example, DuLight, is an AI interface that helps blind or vision-impaired people. A camera mounted on a headset or a user's phone can scan bills, train schedules, labels on boxes, or just about anything; the objects or words are then identified, using deep-learning algorithms and the processor on a mobile phone, and translated into speech that the user hears through an earpiece. "The facial recognition function is also getting really good," says Gu.

Gu's vision of the future is one in which people can enjoy the benefits of technology without being captive to cords and notification buzzes. "I want to bring humans back to an unplugged age," he says.

—Christina Larson

Dinesh Bharadia

MIT Computer Science and Artificial Intelligence Laboratory

A seemingly impossible radio design will double wireless data capabilities.

Dinesh Bharadia invented a telecommunications technology that everyone said would never work: he found a way to simultaneously transmit and receive data on the same frequency.

Because the signal from broadcasting a radio transmission can be 100 billion times louder than the receiving one, it was always assumed that outgoing signals would invariably drown out incoming ones. That's why radios typically send and receive on different frequencies or rapidly alternate between transmitting and receiving. "Even textbooks kind of assumed it was impossible," Bharadia says.

Bharadia developed hardware and software that selectively cancel the far louder outgoing transmission so that a radio can decipher the incoming message. The creation of the first full-duplex radio, which eventually could be incorporated into cell phones, should effectively double available wireless bandwidth by simply using it twice. That would be a godsend for telecom companies and consumers alike.

Bharadia took a leave of absence from his PhD studies at Stanford so he could commercialize the radio through the startup Kumu Networks. Germany-based Deutsche Telekom began testing it last year, but since Bharadia's prototype circuit board is too large to fit in a phone, it will be up to other engineers to miniaturize it. *—Ryan Cross*

COURTESY OF JIAWEI GU; ADAM DETOUR

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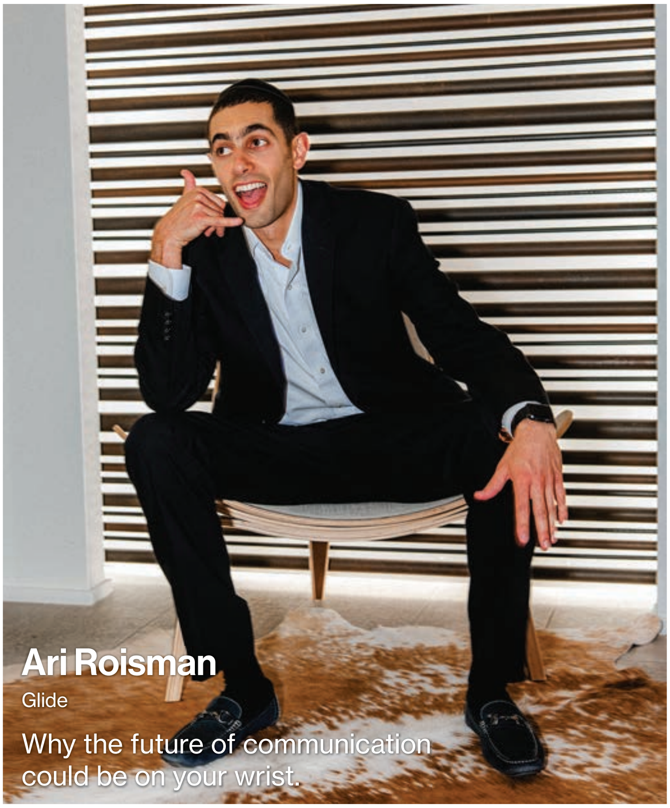
LEMELSON-MIT

Entrepreneurs

Meet seven people who hope to turn innovations into disruptive businesses.

Featuring

Ari Roisman / Stephanie Lampkin / Christine Ho / Meron Gribetz / Samay Kohli / Heather Bowerman / Kelly Gardner



Ari Roisman

Glide

Why the future of communication could be on your wrist.

Roisman believes video messaging will flourish on watches, whose screens are too tiny for typing.

Ari Roisman clearly covets human connection. Minutes after meeting me, the 32-year-old CEO of Glide gladly settles into a conversation about the role of Judaism in his life and how he gave up a promising career in clean energy to move to Jerusalem. "My entire consciousness of this world is that it is a gift," he says, intently.

Since 2012, Roisman has been striving to create a more human alternative to text messaging. Rather than typing short messages on tiny smartphone keys, sometimes adding emojis in a desperate stab to impart nonverbal emotion, you can use Glide's app to send video messages with a single button push. To illustrate, Roisman shows a Glide message he sent to his mother, featuring his daughter singing at a kindergarten event with the seriousness of a brain surgeon. Mom quickly responded with a video of herself laughing at the performance. "If we're going to be glued to these devices, at least we should be connected in a way that is more authentic," he says.

A few million people are using Glide, he says, but that's a pittance in social networking, especially as Instagram and Facebook pour millions into their own video-messaging plans. Glide laid off 25 percent of its staff this spring.

Roisman says he scaled back on marketing and customer service to ensure his startup's staying power. He wants the company to focus on a technology he says will make visual messaging the primary mode of communication: the smart watch. He is convinced that having a small screen just a wrist away will do for video messaging what the PC did for e-mail. —*Peter Burrows*

DAMIEN MALONEY

Stephanie Lampkin

Blendoor

She sees a way to make Silicon Valley's workforce look more like the rest of society.

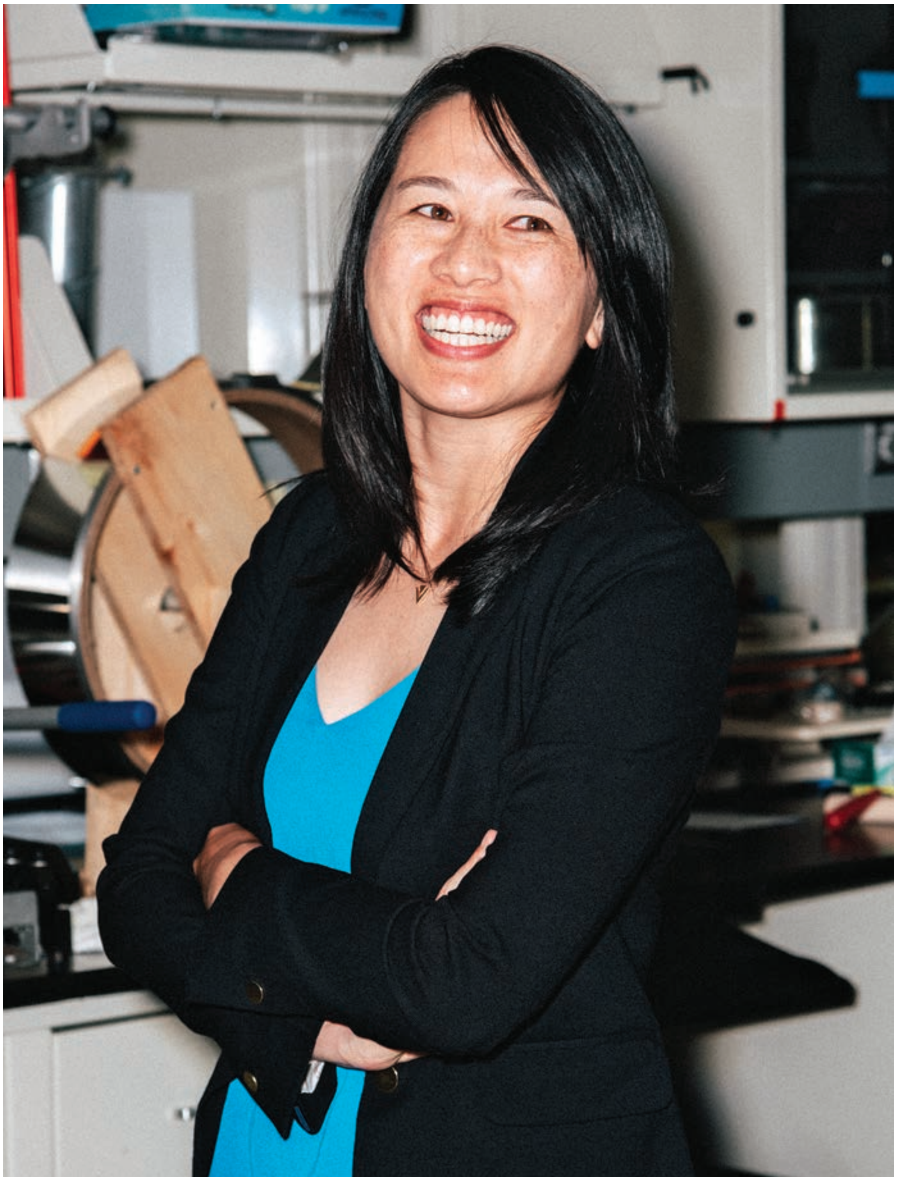
When Stephanie Lampkin applied for an analytics job at a major tech company, she was offered a position in sales instead. To her, this was evidence of bias; she had a degree in management science and engineering from Stanford and had held other engineering positions. Whether or not her race or gender played a role (she is African-American), there's evidence that recruiters often make initial judgments that have little to do with qualifications. A 2014 study concluded that a foreign-sounding name on a résumé could hurt the applicant's chances of even getting an interview.

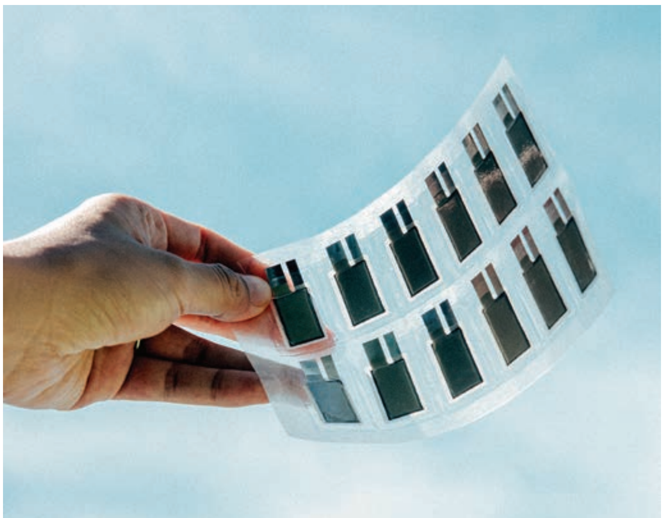
So Lampkin declined the sales job and sat down to code Blendoor, a job-search platform that hides the candidates' names and photos during the initial stages of the process. So far more than 5,000 people have signed up, and the platform is being used by recruiters at Twitter, Airbnb, Facebook, Google, Microsoft, and Intel.

Lampkin hopes Blendoor chips away at the lack of diversity in Silicon Valley. "We've identified the greatest need with large tech companies," she says. But while early users tend to be women and minorities, she says, "we want this to become a de facto recruiting tool for everyone."

—David Talbot

TIMOTHY O'CONNELL





Ho says devices using Imprint Energy's batteries could appear by 2018. The company is working with manufacturers to screen-print batteries on sheets like this one.

Christine Ho

Imprint Energy

Her startup is commercializing thin, flexible, printable batteries that she developed at UC Berkeley.

You say we'll want Imprint Energy's zinc batteries for wearable electronics, health-monitoring patches, and small sensors. Why can't we put existing batteries into such devices?
A lot of these batteries need a lot of plastic housing or metal housing. They need protective circuitry. Because you're doing everything you can to tame a very, very wild and reactive system. What's interesting about Imprint's approach is we're using an inherently more stable chemistry that doesn't need that hermetic sealing. [That results in] the packaging being much more simplistic and thinner. What's nice about zinc batteries is the materials are really cost-effective and easy to acquire. They're also nontoxic.

Why isn't zinc already widely used to power electronics?
There's usually a very nasty corrosive electrolyte used [with it]. Especially for on-body applications, you don't want to put in something nasty like that. The other thing is, zinc is not traditionally a rechargeable system.

How did you get around those issues?
Batteries are stacked; they look like a stacked sandwich. The middle layer, like the jelly in the jelly sandwich, is called the electrolyte. What I realized was that if we eliminated that and replaced it with something that is stable with the zinc system and rechargeable, we could open up a whole new market space. I looked at lots of different materials, literally throwing everything in a bucket and hoping that it worked. We started to get some really interesting results with one of these material sets we were looking at. We could basically take this material and cast it into a solid film. So you could cut it, you could stretch it and whatnot, but inside it had ions that moved. *—Rachel Metz*

TIMOTHY O'CONNELL

Meron Gribetz

Meta

An augmented-reality dreamer tries to turn his vision into a business.

Meron Gribetz has a hard time sitting down when he's talking about his augmented-reality startup, Meta. Grinning, he stands or paces as he explains that he had always wanted to create a way to bring digital information into the real world to make it easier to absorb. Then in 2011, sunlight shimmering through an airplane window hit the lens of his sunglasses and made him realize how he would do it.

Since then, he's managed to raise $73 million in funding to go up against rivals like Microsoft and its HoloLens device. Why the excitement?

This year, Gribetz unveiled the company's latest headset, the Meta 2, which sells for less than a third of what the HoloLens headset is going for. It lets you do things like grab and prod 3-D imagery with your hands, or conduct a video call with another Meta user, who can hand you a virtual object that you can then inspect from any angle.

$949

PRICE OF THE META 2

Both the Meta and the HoloLens are aimed at software developers, who will have to come up with applications. But Gribetz, who was raised in Israel by American parents, is aggressively optimistic about the technology because he thinks it will let us ditch devices like laptops, smartphones, and tablets for one super-mobile package. Within five years, he imagines, AR headsets will be reduced to a strip of glass over your eyes that's "nearly invisible."

Meta is building software meant to be more intuitive to navigate than windows and icons. Gribetz believes so deeply in AR's promise, in fact, that he's pushing his own employees to stop using computer monitors and mouses with their laptops by next spring; instead, the company will rely on Meta 2 and its hand-tracking capabilities to help them get their work done.

—Rachel Metz

Gribetz models the Meta 2 headset, which weighs about a pound and a half.

DAMIEN MALONEY

Two of GreyOrange's Butler robots, which are designed to be warehouse workhorses.

Samay Kohli

GreyOrange

Look out, Amazon: after greasing the wheels of India's e-commerce boom, this executive eyes overseas expansion.

Homegrown e-commerce companies in India are slashing prices and delivery times as they battle to serve the country's burgeoning middle class. Many of these companies are able to do it because of warehouse automation technologies developed by Samay Kohli and his team at the robotics firm GreyOrange.

GreyOrange sells swarms of "Butler" robots, which store products and bring shelves to human workers, and "Sorters," which automatically scan and sort packages of any size or shape. The company boasts 92 percent of India's warehouse automation market, a sector that Kohli thinks "can become humongous."

With offices in Hong Kong and Singapore, the company isn't content serving India alone. It plans to expand into the Middle East and China this year, and within two years Kohli expects to be exporting warehouse robots to Europe. He hopes to get a first-mover advantage over other robotics startups chasing the same opportunity—one that became even larger after Amazon bought the warehouse automation company Kiva Systems in 2012 and brought its technology in house rather than selling it to Amazon's e-commerce rivals.

25%

PORTION OF GREYORANGE'S REVENUE THAT GOES TO R&D

Kohli and his cofounder Akash Gupta launched the company in 2011, after developing, while in college, what they believe to be India's first humanoid robot. Seeing China's e-commerce boom, they spotted "an industry ripe for disruption," says Kohli.

—Edd Gent

Heather Bowerman

Dot Laboratories

Cheap hormone tests could begin to address gender disparities in health care.

Problem

"There are significant differences in the ways that men and women experience many diseases and drugs, and until this problem is solved, women will be forced to make do with therapies that may be of limited benefit," says Heather Bowerman.

For example, hormones cause plaque to form differently in the arteries of men and women. Yet drugs to treat cardiovascular disease are tested disproportionately on men, and as one consequence, their death rates from that illness are declining faster than women's. Detailed hormonal data could help doctors tailor drugs and treatment regimens so that they work better for women.

Solution

Bowerman is CEO of a startup, Dot Laboratories, that is developing a cheap and easy way to test female sex hormone levels and track them online. A patient spits into a tube at specific times and mails the tubes to Dot Laboratories. The company then delivers data on hormone levels in an app for the woman or her doctor to review. It's still in a beta test; the company plans to publish data on the efficacy of its methods and release the diagnostic product in 2017.

Developing more drugs that take hormonal changes into account will take time. Even so, Anula Jayasuriya, a doctor who invests in life sciences companies, says such tests will help end the "sex bias in basic research and clinical medicine."

—David Talbot

COURTESY OF SAMAY KOHLI ; COURTESY OF HEATHER BOWERMAN

TIMOTHY O'CONNELL

Kelly Gardner

Zephyrus Biosciences

This bioengineer figured out how to handle a key challenge facing biotech startups.

Your company makes a test that can measure protein levels in single cells. Why is this important?
Proteins are the functional molecules of the cell. Measuring them is vital to understanding and targeting disease. But they're much more challenging to measure than DNA because they can't be amplified—you have to measure the molecules that are actually in the cell.

Measuring proteins in single cells could help us understand a tumor. Are all the cells in a tumor going to be targeted by a drug, or do some of them lack the drug target? Which cells will metastasize?

Who uses your test?
Right now we're focused on the research market. Before we started our product development, we interviewed over 100 biomedical researchers to find out what applications people were interested in, and designed our hardware to meet that need.

You say you followed the “lean startup” model, which comes from the software industry. Why did you adopt it?
You see a lot of academic publications that are innovative, but they never make it out of the lab. One barrier is the willingness of investors to fund early-stage biotech companies. Life sciences startups can be incredibly expensive. We did it with only $1.8 million in private and public funding and seven employees. We were acquired by ProteinSimple [a division of a public company called Bio-Techne] this spring, after two and a half years.

Are you already antsy to start another company?
I'm an entrepreneur at heart, and in the Bay Area it's hard not to be distracted by shiny things. But it's important for me to make sure this technology is successful.

—Katherine Bourzac

Pioneers

Pushing the edge of science, these innovators are creating new approaches to tackling technology challenges.

Featuring

Aleksandra Vojvodic / Jia Zhu / Yihui Zhang / Qing Cao / Oriol Vinyals / Ying Diao / Vivian Ferry / Sergey Levine

Aleksandra Vojvodic

University of Pennsylvania

A computation whiz speeds up the search for catalysts that will make green chemistry possible.

Using enzymes honed over hundreds of millions of years of evolution, plants readily split water into oxygen and hydrogen that's used to fuel metabolic reactions. Humans, too, could use hydrogen as a fuel and a way to store energy from intermittent renewable sources. But we don't have millions of years to figure out how to make practical catalysts.

Aleksandra Vojvodic uses supercomputers to design new catalysts for water splitting and other reactions. The idea behind her work, she explains, is to "circumvent the trial and error of nature"—and of the chemistry lab.

Splitting water requires two catalysts, one for making hydrogen and the other for making oxygen. "The things that work efficiently are usually rare or expensive," says Vojvodic. That's where computational chemistry comes in. To predict the behavior of a catalyst, Vojvodic makes computer models that relate a material's functions to its structure using the rules of quantum mechanics. Chemists know what functions the catalyst needs to have, and they know how different kinds of atoms and structures are likely to behave. Vojvodic's computer experiments, at the SLAC National Accelerator Lab, have yielded oxygen-producing catalysts that match or outperform those made of expensive materials.

Researchers have been using powerful computers to try to design better catalysts for years, with varying degrees of success. But today's supercomputers are now capable of doing much more complex calculations. And Vojvodic has been exceptionally talented at taking advantage of computing power; identifying new ways to represent electronic properties, chemical structure, nanostructure, and other properties in mathematical calculations; and writing programs to carry them out. Working with experimentalists, she and her coworkers have recently made extremely efficient water-splitting catalysts that her modeling work predicted. The researchers are now eyeing other catalysts, including ones that can convert nitrogen and other abundant molecules into useful chemicals.

—Katherine Bourzac

The idea behind her work, she explains, is to "circumvent the trial and error of nature"—and of the chemistry lab.

RC RIVERA; COURTESY OF JIA ZHU

Jia Zhu

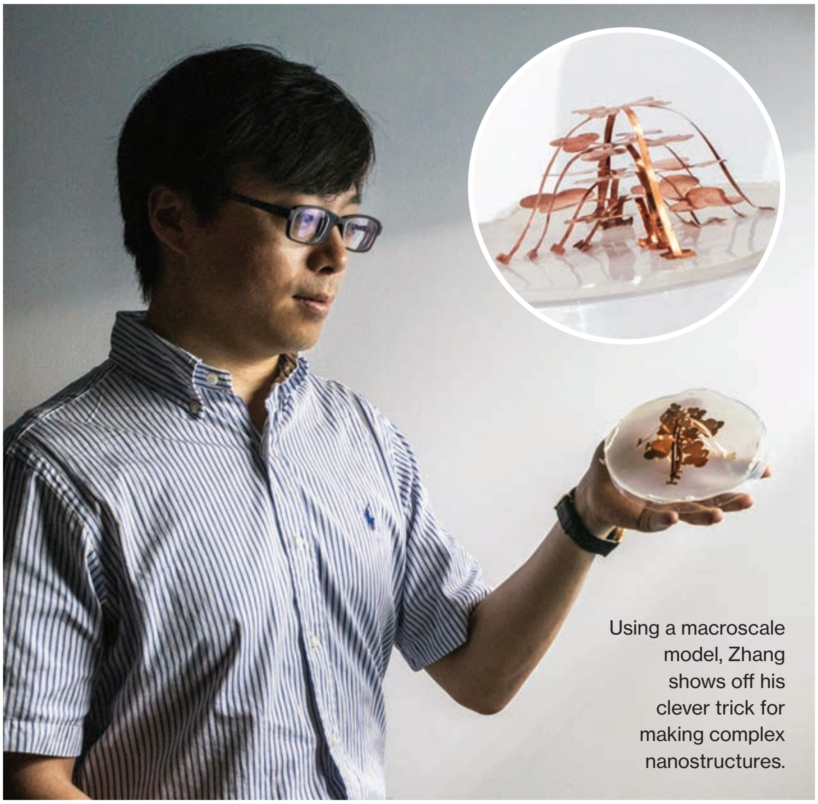
Nanjing University

What to do if there is no clean water around.

Water is everywhere; safe drinking water is not. So Jia Zhu has created a thin metal sheet capable of floating on the surface of a body of water, absorbing lots of sunlight and using the energy to generate steam that condenses into clean water. "It only needs two things. The first is water—no matter what kind of water you have—and the second is the sun," says Zhu.

The device could be used to desalinate seawater or treat polluted water: after the water is turned into steam, what's left are salts or solidified contaminants that can be easily collected.

He also envisions other ways to put the ingenious apparatus to use. "The steam doesn't have to be condensed," he says, suggesting that it could be used to produce power. *—Yiting Sun*



Using a macroscale model, Zhang shows off his clever trick for making complex nanostructures.

Yihui Zhang

Tsinghua University

Pop-up nanostructures make it far easier to fabricate very tiny shapes.

Yihui Zhang likes to invite visitors to his office to stretch a piece of highly elastic silicone that has a soccer-ball-like structure attached to it. Once the silicone is pulled taut from four corners, the three-dimensional structure becomes a two-dimensional pattern that looks like a wheel with many adjacent hexagons and pentagons in the center. When the silicone is relaxed again, the flattened pattern pops back into its three-dimensional shape.

With this trick, Zhang has solved the challenge facing many researchers: how to fabricate complex three-dimensional nanoscale structures. Although the demonstration is done at the macro level, the idea works with nanostructures, too: easily created two-dimensional patterns can be attached to a substrate stretched taut and then buckled into three-dimensional structures as the substrate is relaxed. This process works with a wide range of materials such as metals and polymers.

Easily created two-dimensional patterns buckle into three-dimensional structures as the substrate relaxes.

The technique could be used to create nanostructures for a variety of uses. Ultimately, Zhang hopes to develop a database or algorithm that allows researchers to easily map the three-dimensional structures they want onto two-dimensional precursors. “It’s a tool,” he says. “People from different disciplines can build their own innovations.” —*Yiting Sun*

Qing Cao

IBM Research

His inventions are helping IBM in its decade-plus quest to replace silicon transistors with more efficient carbon nanotubes.

2001	IBM researchers devise a way to produce arrays of carbon-nanotube transistors.
2002	IBM researchers show that nanotube transistors can carry more than twice the electric current of top-performing silicon transistor prototypes. This is interpreted as the first evidence that nanotubes can outperform silicon transistors.
2006	The first integrated circuit using a single carbon nanotube is built at IBM.
2008	During his doctoral studies at the University of Illinois, Qing Cao invents a way to print circuits of nanotubes on flexible plastic substrates.
2013	At IBM, Cao develops a technique that applies mechanical force to push purified nanotubes in water together into high-density, neatly ordered arrays.
2015	Cao overcomes a fundamental roadblock to commercially viable nanotube transistors. He devises a way to connect metal wires to carbon nanotubes by welding metal atoms to the nanotubes’ ends.
2016	IBM incorporates carbon nanotubes into its in-house semiconductor research line to figure out how to refine and scale up the technology.
2020–2025	IBM aims to have its nanotube transistors ready to replace silicon transistors. The company estimates that nanotube transistors will perform two to three times better than silicon and require half as much power.

—*Elizabeth Woyke*

GILLES SABRIE

Cao at IBM's Watson Research Center. At bottom right he holds a silicon-based wafer with carbon-nanotube devices.

JACKSON KRULE

JESS KOHL

Oriol Vinyals

Google DeepMind

Showing computers how to learn might seem like a game, but it's also serious business.

When he was 15 years old, Oriol Vinyals became obsessed with StarCraft, a video game in which three factions vie for control of the map—like chess if it were played not only with black and white pieces but also with red ones. Vinyals soon became the top-ranked player in Spain. "I almost knew the game would return later in my life," he says. "I was fascinated by the artificial-intelligence problems it presents."

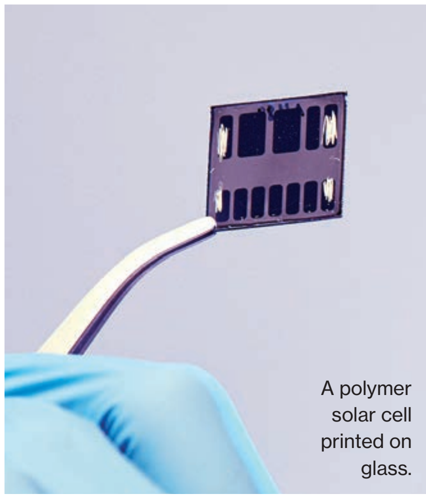
It was more than a decade before Vinyals's premonition came to pass. While he was studying at UC Berkeley, he helped to create an AI bot that was able to play StarCraft unassisted. The bot, forebodingly dubbed Overmind, represented a triumph in machine learning.

Later, while he was working on the Google AI team creating new techniques for language translation, inspiration struck. Vinyals decided to see whether a computer could accurately write a description of an image. It's a form of translation, albeit from pixel to caption. "I remember it so well," he says. "I changed a single line of code: instead of translating from French, I changed my code to input an image instead." The next day, Vinyals showed his program a photograph of a busy market stall, the ground beside it littered with bananas. The caption read: "A group of people standing in the market buying fruits." "It worked!" he recalls. "It wasn't just saying 'People on the street.' It was reading the image with sophistication." The technology, now being incorporated into Google Image Search, allows computers to caption images and show them to people who enter relevant search terms.

While he was working on the Google AI team, creating new techniques for translation, inspiration struck.

Vinyals and his coworkers have developed a technology now used in Gmail called Smart Reply, which automatically suggests short replies to e-mails. And now, having joined the team at Google DeepMind in London, he has come full circle. There, he is working to create computers that can teach themselves how to play and win complex games—not by hard-coding the rules but by enabling them to learn from experience.

—*Simon Parkin*



A polymer solar cell printed on glass.

SETH LOWE

Ying Diao

University of Illinois

She knows how to print perfect plastic solar cells.

Problem

Flexible solar cells that are cheap to make could be "printed" on many surfaces, even windows. But the polymers that would be required have so far been lackluster at converting sunlight to electricity. One reason is that unlike more efficient solar materials such as crystalline silicon, polymer-based materials have a messy molecular structure that looks like cooked spaghetti.

Solution

Ying Diao is creating printing techniques that bring order to the otherwise chaotic assembly of plastic molecules. She has made organic solar cells with double the efficiency of previous ones. Diao came up with a microscopic "comb" that controls the flow of the molecules and lets them assemble into orderly structures during printing. —*Ryan Cross*

Vivian Ferry

University of Minnesota

She uses nanocrystals to trap light and increase the efficiency of solar cells.

With her hands cloaked in aquamarine rubber gloves, Vivian Ferry, an assistant professor of chemical engineering and materials science, picks up a lipstick-size test tube filled with clear liquid. When she shines UV light through the tube, its contents turn a glowing shade of fluorescent orange. Tiny crystals suspended in the liquid explain the vial's fiery glow: they absorb high-energy blue wavelengths and emit lower-energy reds.

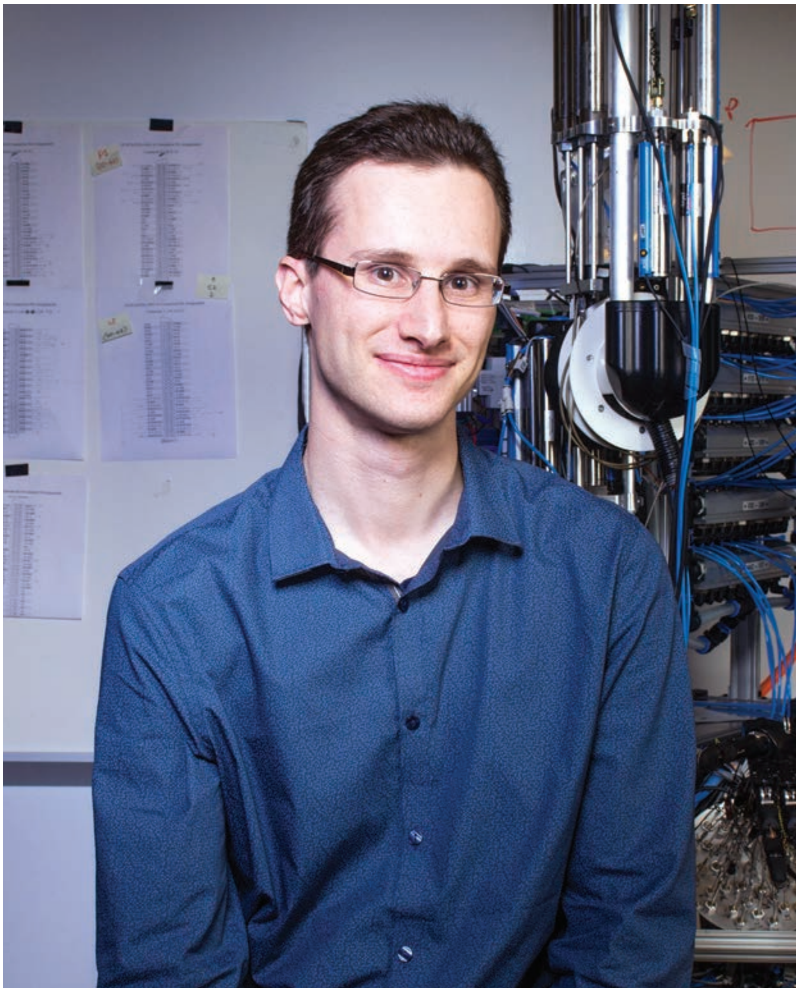
Existing solar cells tend to absorb limited wavelengths of light, letting most of the sun's energy pass through uncaptured. If solar cells could grab more light, they would generate more electricity and make solar power even cheaper. So in addition to the luminescent crystals, Ferry turned to tiny mirrors made of nanostructured metals that can trap specific wavelengths and steer light toward the solar cell.

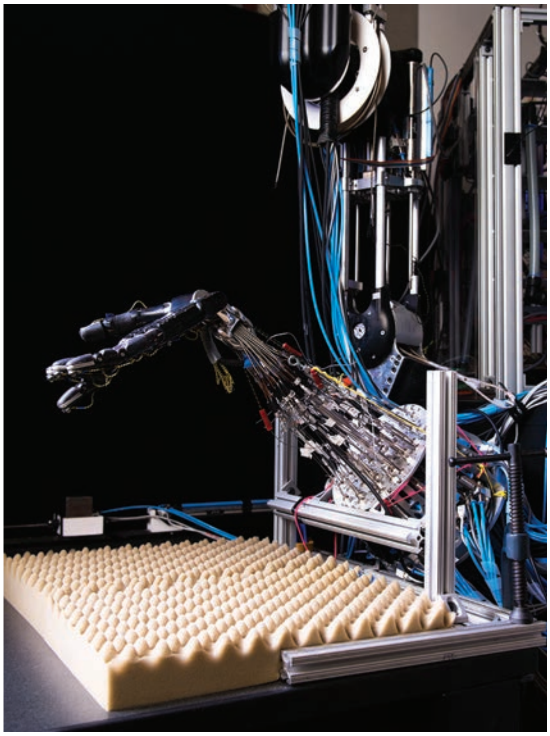
For now, Ferry makes her luminescent nanocrystals with cadmium selenide and cadmium sulfide, neither of which is ideal since cadmium is a toxic metal. But her improvements—and subsequent drops in cost—stand to become so significant that the technology could still work well using substances that are more abundant and less toxic.

—Emily Sohn

If solar cells could grab more light, they would generate more electricity and make solar power cheaper.

HUNT AND CAPTURE





Sergey Levine has demonstrated that his algorithms can help a robotic arm teach itself how to manipulate various objects.

DANIEL BERMAN

Sergey Levine

University of California, Berkeley

He teaches robots to watch and learn from their own successes.

While serving a nine-month stint at Google, Sergey Levine watched as the company's AlphaGo program defeated the world's best human player of the ancient Chinese game Go in March. Levine, a robotics specialist at the University of California, Berkeley, admired the sophisticated feat of machine learning but couldn't help focusing on a notable shortcoming of the powerful Go-playing algorithms. "They never picked up any of the pieces themselves," he jokes.

One way that the creators of AlphaGo trained the program was by feeding 160,000 previous games of Go to a powerful algorithm called a neural network, much the way similar algorithms have been shown countless labeled pictures of cats and dogs until they learn to recognize the animals in unlabeled photos. But this technique isn't easily applicable to training a robotic arm.

So roboticists have instead turned to a different technique: the scientist gives a robot a goal, such as screwing a cap onto a bottle, but relies on the machine to figure out the specifics itself. By attempting the task over and over, it eventually attains the goal. But the learning process requires lots of attempts, and it doesn't work with difficult tasks.

Levine's breakthrough was to use the same kind of algorithm that has gotten so good at classifying images. After he gives the robot some easy-to-solve versions of the task at hand—instructing it to screw on the cap, for example—the robot then retrospectively studies its own successes. It observes how the data from its vision system maps to the motor signals of the robotic hand doing the task correctly. The robot *supervises its own learning*. "It's reverse-engineering its own behavior," Levine says. It then can apply that learning to related tasks.

The robot observes how the data from its vision system maps to the motor signals of its hand.

With the AI technique, previously insoluble robotics tasks have suddenly become approachable, thanks to the massive increase in training efficiency. Suddenly, robots are getting a lot more clever.

—Andrew Rosenblum

Humanitarians

They are taking unconventional routes to bring about a healthier, cleaner, and more adaptable world.

Featuring

Sonia Vallabh / Ehsan Hoque / Ronaldo Tenório / Jagdish Chaturvedi / Kelly Sanders

Sonia Vallabh

Broad Institute

A devastating personal diagnosis led her to become a scientist on the trail of a cure.

Five years ago, Sonia Vallabh graduated from Harvard Law School and went to work at a small consulting company. But a stunning medical diagnosis made her change course completely: she learned she has a genetic mutation that causes a deadly brain disease. Today she and her husband work in a lab at the Broad Institute of MIT and Harvard and have published research showing a possible pathway to a treatment. As she told the tale at an event on precision medicine with President Obama in February:

"At the heart of my story is a single typo in my genome.

"We all carry around thousands of typos in our DNA, most of which don't matter much to our health—but my typo is an unusually clear-cut case. It's a single change in a particular gene that causes fatal genetic prion disease, where patients can live 50 healthy years but then suddenly fall into deep dementia and die within a year. And there's no treatment—at least, not yet.

"In 2010, I watched this disease unfold firsthand. I had just married my husband, Eric Minikel. My mom, healthy at 51, had single-handedly organized our beautiful wedding. Then, all of a sudden, we were watching her waste away before our eyes. We had no name for what we were seeing. It was only from her autopsy that we learned there was a 50 percent chance I'd inherited the genetic mutation that killed her.

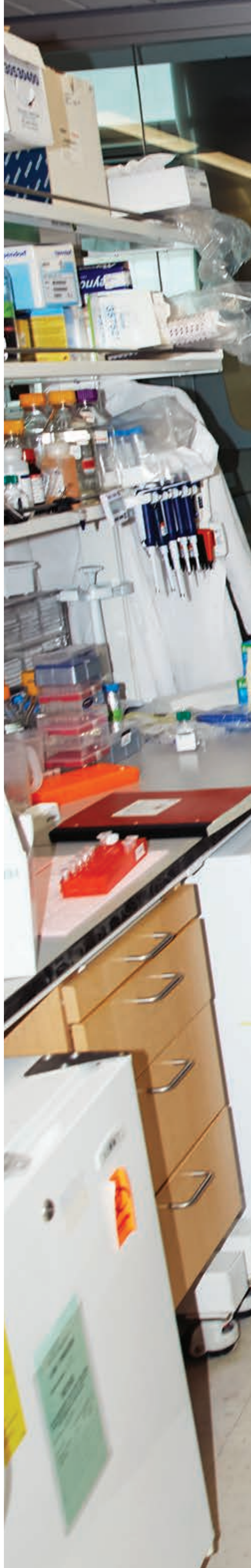
"Knowing the hard truth has given us a head start against our formidable medical enemy."

"We decided right away I'd get tested. We wanted to know what we were up against. After months in agonizing limbo, a geneticist confirmed our greatest fear: *The same change that was found in your mother was found in you.*

"Knowing the hard truth has given us a head start against our formidable medical enemy. We waged a campaign to educate ourselves—taking night classes, attending conferences, and eventually taking new jobs in research labs. We retrained as scientists by day and applied what we were learning to understanding my disease by night. Four years later, we're devoting our lives to developing therapeutics for my disease.

"We know the road ahead is uncertain—no amount of hard work can guarantee there will be a treatment for me when I need one. We are going to do everything we can, hand in hand with creative allies from every sector, to build this bridge as we walk across it and develop a treatment that could save my life, and the lives of many others."

—Antonio Regalado



LEONARD GRECO

Vallabh and her husband, Eric Minikel, in the lab where they are in a race to solve puzzles of prion disease.

Ehsan Hoque

University of Rochester

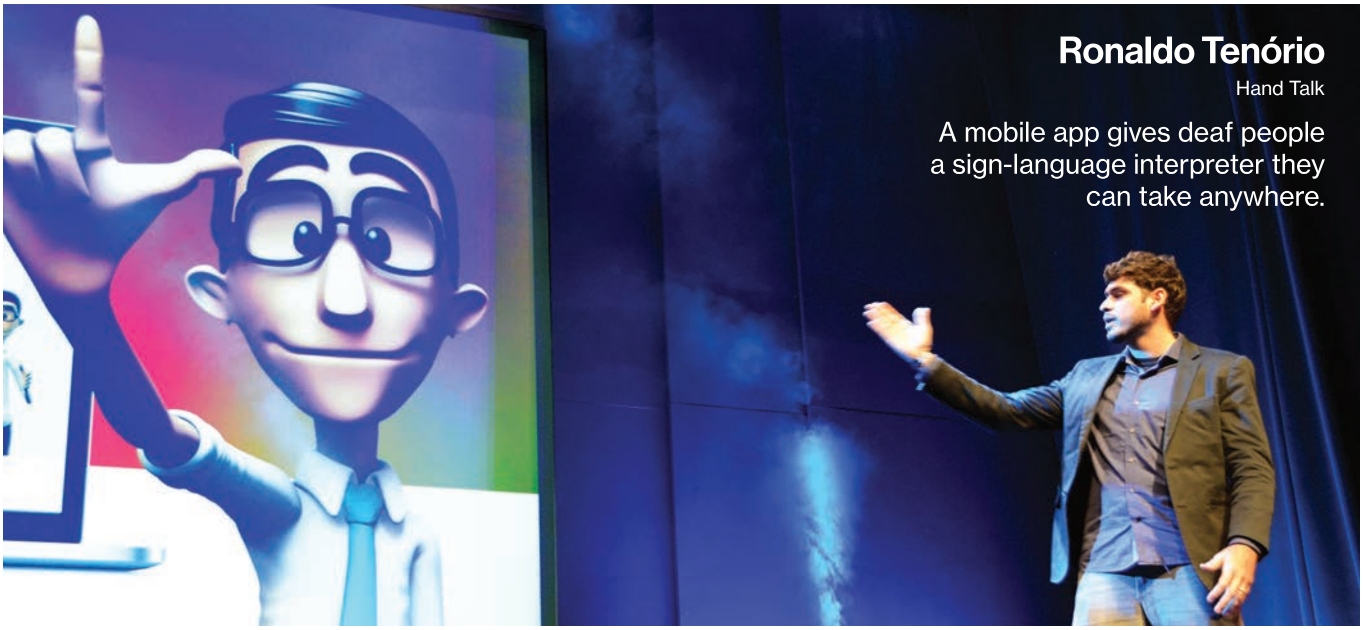
If you want to be the life of the party, practice by talking to a machine first.

Can computers teach us to be our best selves? Ehsan Hoque, a researcher at the University of Rochester, believes so. He has created two computer systems that train people to excel in social settings.

One program has a virtual businesswoman that can recognize your expressions and statements so she can nod, smile, and prompt you with further questions as you chat with her. At the end of the conversation she'll give you feedback about your interpersonal performance, including your body language, intonation, and eye contact.

Hoque also designed a pared-down mobile version, free for anyone with Internet access to use. There's no animated character; instead, it records video and sends you a write-up about your social skills, noting the speed of your speech, the pitch and loudness of your voice, the intensity of your smiles, and whether you overused certain words.

All of Hoque's research comes back to his brother, a teenager with Down syndrome. Hoque is his brother's primary caretaker and has seen how difficult social interactions of any kind can be for him, especially in school. But Hoque hopes his tools will be useful to all kinds of people—individuals with Asperger's, customer service representatives, nervous students with looming class presentations, or even just someone gearing up for a date or an interview. *—Julia Sklar*



Ronaldo Tenório

Hand Talk

A mobile app gives deaf people a sign-language interpreter they can take anywhere.

A deaf person walks into a bar. That isn't the beginning of a joke, but a potentially frustrating situation—unless the bartender happens to know sign language. That's where Hand Talk comes in. It translates spoken words into sign language that an avatar then conveys on a smartphone screen.

For now, Hand Talk can only translate Portuguese into Libras, the sign language used in Brazil—the home of the program's creator, Ronaldo Tenório. But Brazil alone has at least 10 million deaf people, one million of whom have downloaded Hand Talk's mobile app.

6 million

NUMBER OF MONTHLY TRANSLATIONS ON HAND TALK

The users hold up their smartphone to a hearing person, who sees a message on the screen that says "Speak to translate." As soon as the person starts talking, an animated avatar named Hugo begins signing.

Turning the audio into animations of gestures requires laborious programming because everything has to be exactly right, all the way down to Hugo's facial expressions, which also carry meaning in sign language. Tenório and his team feed their program thousands of example sentences every month and match them with 3-D animations of sign language. They constantly push these improvements out through app updates.

Tenório plans to roll out different versions of the avatar in the future so users can switch the gender or race of their Hugo in an effort to broaden the appeal and accessibility of having a virtual translator in one's pocket.

—Julia Sklar

COURTESY OF EHSAN HOQUE; COURTESY OF RONALDO TENÓRIO

Jagdish Chaturvedi

InnAccel

This doctor can laugh about the complex path he took to becoming an innovator.

"I invented a low-cost ear, nose, and throat—ENT—imaging device. So I call myself the first ENTrepreneur! Sorry—cheesy joke; I'm also an amateur standup comedian. I love performing. It's how I de-stress. But I also find comedy helps sharpen my observational skills.

"Those skills helped me invent Entraview, which has helped 200,000 patients. As a trainee doctor I saw many farmers with advanced throat cancer. I discovered that expensive imaging systems were only available in major cities, so rural doctors relied on outdated mirrors and headlamps. I asked my boss why no one had tried attaching endoscopes to small off-the-shelf cameras. He said, 'Why don't you?'

"Entraview was a big learning curve for me. I worked with a design firm but got too involved trying to create a one-size-fits-all device. I'd nearly exhausted my funds when my boss said, 'Go learn the right way to do this.'

"The Stanford-India Biodesign program teaches Indian doctors and engineers how to invent. Their process showed me where I'd gone wrong and gave me the connections to arrange a pitch with Medtronic. We simplified and focused on ears. Not the original goal, but the path of least resistance to market, and now the platform can evolve.

"I've since contributed to 18 medical-device inventions, and I'm now clinical lead at a med-tech incubator, InnAccel, where I help multiple startups while still practicing medicine, to keep me grounded with clinical needs.

"India imports 75 percent of its medical tech. We have great inventors, but most make the same mistakes because they don't get the innovation process. The first step is finding the right team."

—as told to Edd Gent

Top two images: Chaturvedi advises a patient's relatives and uses an early version of the Entraview to examine a man's ear in Bangalore. Bottom: The prototype attached to an off-the-shelf camera.

SAMYUKTA LAKSMHI

Kelly Sanders

University of Southern California

A researcher in drought-ridden California tries to better account for the ways we use water.

Just about all power plants use water in some way—primarily for cooling. In fact, generating electricity accounts for about 40 percent of all the fresh water that is drawn from reservoirs, rivers, and other surface sources in the United States. Kelly Sanders, an assistant professor of civil and environmental engineering at the University of Southern California, has developed new methods of analyzing the complex relationship of water and energy—and is showing how both resources can be managed more wisely.

Although power plants typically return water to the source after it runs through cooling systems, those withdrawals and returns can be disruptive to the environment. Many newer coal and natural-gas plants reuse water in their cooling systems so they do not need to withdraw as much of it from reservoirs and rivers, but in the process they lose more water to evaporation. And that means, as Sanders has highlighted, that many newer plants end up consuming more water overall. She also looks carefully at the water individual nuclear power plants use to keep from overheating and causing a meltdown. If the water source gets too warm and must cool down before it can be used, forcing the power station to scale back production, are the costs of the plant being miscalculated?

Having reframed how we measure water and energy usage, Sanders is becoming influential in policy and planning. She briefed Congress as it considered the Nexus of Energy and Water for Sustainability Act, which takes initial steps to have the federal government measure water usage not just in gallons but also in units of energy. "We select our power based on price," she says, "but how do we define what's cheap?" —*Ryan Bradley*

DAMON CASAREZ

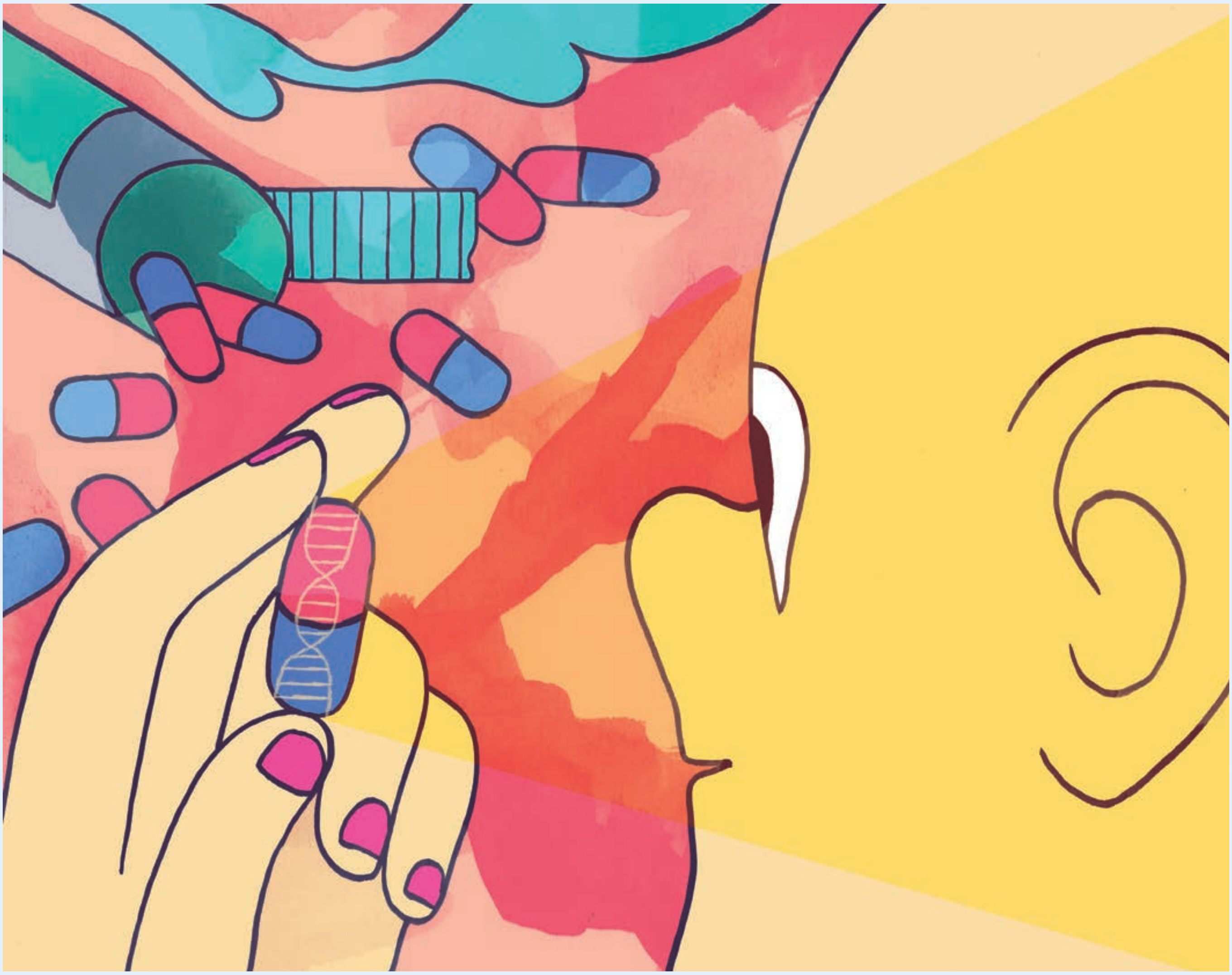
Sanders has developed better ways of quantifying the energy it takes to supply water—and vice versa.

MIT Technology Review
BUSINESS REPORT

CONTENTS

Precision Medicine

A wave of scientific breakthroughs and financial investment might finally usher in an era of precisely individualized health care.



PATRICK KYLE

The Big Question

Slow Progress to Better Medicine

Thirteen years after the human genome was sequenced, some remarkable treatments are being developed.

● As soon as Carina was born on July 25, 2014, it was clear something was wrong. The midwife pointed it out: a lump on the right side of her jaw. At first doctors were unable to make a diagnosis, but in time it was discovered to be a pernicious form of cancer that would, over the first year and a half of Carina's life, resist eight rounds of chemotherapy and multiple surgeries.

Last October after yet another surgery, when the tumor again began to grow, Carina's parents, Joe and Christie, found themselves running out of options. Radiation was a possibility, but there was a significant danger of brain damage. Radiologists advised them to first try any experimental drug they could find.

Genetic testing done on the tumor showed an abnormal fusion of two genes. This fusion seemed to be creating growth signals that were leading to cancer, and Carina's oncologist, Ramamoorthy Nagasubramanian of Nemours Children's Hospital, found that a medicine designed to interfere with a protein made by that fusion was in clinical trials for adults. He contacted the drug maker, Loxo Oncology, and together they appealed to the U.S. Food and Drug Administration to allow a pediatric trial. In December, Carina became its first patient.

Over the next month, Joe and Christie watched as the tumor shrank. It was the size of a walnut when the treatment started; 28 days later it seemed to be almost completely gone. Though Carina is not cured—she will continue to take the medicine for as long as it works, and at some point it is likely that the cancer will mutate again—today she is an active, curious two-year-old. The treatment "has bought us happy baby time," says Joe. (To protect their privacy, the family asked that their last name not be disclosed.)

Precision medicine combines data from different sources to create a medical portrait of each person and design targeted treatments.

Carina's case and others like it are the success stories of an approach to medicine that focuses on individual differences in patients' genes, often in combination with information about their environment, health history, and lifestyle. It's called precision medicine, a broad term most often used to describe an approach that combines data from many different sources to create a medical portrait of each person and design more effective, targeted treatments. It's a big shift from our current medical model, which focuses on generic approaches and treatments suitable for as many people as possible, but its potential helped motivate a $215 million investment by the White House to help develop it. That's also why Memorial Sloan Kettering Cancer Center in New York City, a leader in its field, has sequenced 10,000 tumors since 2014 in an effort to provide insight to oncologists developing cancer therapies individualized for each patient.

Like any big shift, this one will involve a lot of challenges to well-established practices across the medical industry, from regulation to drug development.

Which parts of the health-care industry will benefit from this disruption? That is the big question of this Business Report.

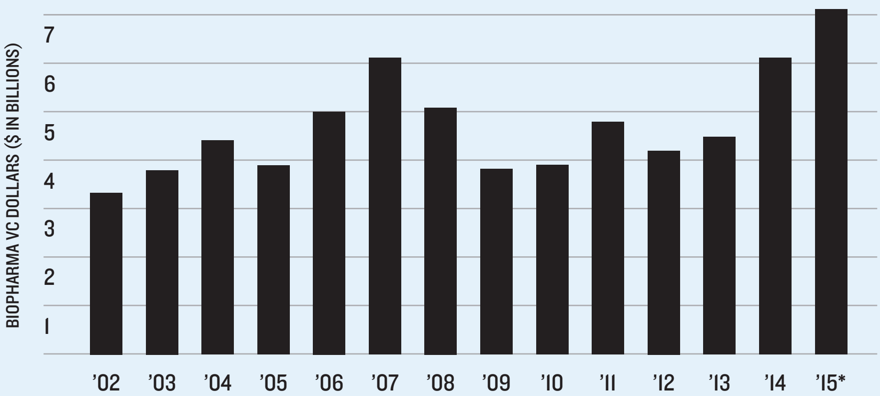
One group already profiting is technology-driven startups. Venture capitalists invested a record $7 billion in U.S. biopharmaceutical startups last year, according to data from Silicon Valley Bank—much of that driven by enthusiasm over new breakthroughs in genetic medicine and other technologies.

Loxo Oncology, maker of Carina's medicine, exemplifies the role smaller companies are playing. Loxo founder Joshua Bilenker says the company has benefited from the new availability of public information in sources like the National Institutes of Health's Cancer Genome Atlas.

Private and public funding has also been available, with Loxo raising approximately $250 million from investors so far. Bilenker says his company's focus on relatively simple genetically driven cancers makes it possible to know quickly if a treatment works or not, welcome news among investors. Treatments can also be tested in smaller groups, at a much lower cost than a large pharmaceutical company incurs developing a medicine for more widespread illnesses. Blockbuster drugs

Money In

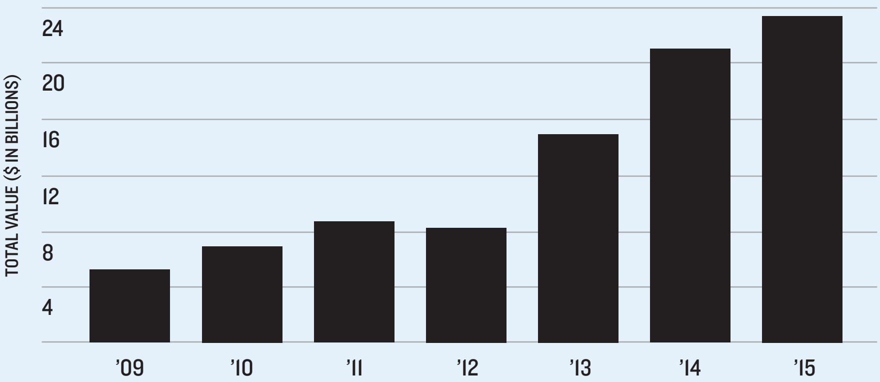
Venture capital investment in biopharma companies is climbing.



SILICON VALLEY BANK
*PROJECTED

Money Out

Estimated investor returns on health-care IPOs, mergers, and acquisitions.



for common ailments typically require large, expensive randomized trials. The condition Carina has, on the other hand, is unlikely to have more than a few thousand sufferers in the U.S.

The hope is that precision medicine will eventually be used to treat major illnesses. But that will be challenging. Those conditions are complex and may not have a clear genomic component.

With smaller groups of patients to treat, targeted medicines are unlikely to produce blockbuster revenues. Companies like Loxo—which has not yet set a price for its drug—will probably need to charge significant amounts per patient to recoup their investment. The average cost of cancer treatment is currently estimated at $10,000 per month, but after a decade of sharp price inflation in cancer drugs, insurers are questioning those prices. So are patients, who increasingly have to pay a significant portion themselves.

There's technological risk as well. Editas Medicine is a company focused on using a new form of gene editing called CRISPR/Cas9 to treat medical conditions driven by genomic disorders. Slated to begin clinical trials next year, the company has a lot of complicated science to perfect before it can hope to be effective—everything from gene editing itself to delivering the therapy effectively into enough of the proper cells.

Beyond knowing more about the genome, precision medicine depends on gathering information about environment, lifestyle, and health history as well. Companies like WellDoc and Omada are trying to find ways to use mobile phones and computers to engage with patients, particularly those with chronic diseases like diabetes and hypertension, in order to record health and lifestyle data and help patients and doctors find insights.

Though some of these programs are successful—Omada reports that 64 percent of its participants are still actively using the system after a year—they have not sufficiently captured patients' attention overall, says Joseph Kvedar, who runs the "connected health" initiative at Partners HealthCare, a leading Boston-area academic health-care system. "We haven't been able to engage people the way Snapchat, Instagram, or Facebook can," he says.

Kvedar acknowledges that a reminder of being sick is never going to be as enjoyable as social media, but there remains a great opportunity, he says: "All your device data, mobile data, all your activities that make you unique—if we can track that and your health, plus your genomic predisposition, there is so much we can do."

—*Nanette Byrnes*

Expert Q&A

The Evangelist of Individualized Medicine

Cardiologist and genomic-medicine expert Eric Topol makes his case for a future of "medical selfies."

● Eric Topol, a cardiologist and professor of genomics at the Scripps Research Institute, is a leading proponent of using DNA analysis and digital technologies to understand each patient as an individual. In addition to using these technologies with his own patients, he works as an advisor to companies including Illumina and Gilead Sciences, and he shares his insights through a Twitter feed that is required reading for those interested in the topic. In his book *The Creative Destruction of Medicine*, Topol describes how the ability to inexpensively sequence an individual genome, combined with new health applications made possible by wireless technology, can make medical care more customized and effective. He spoke to Business Reports senior editor Nanette Byrnes by phone from La Jolla, California.

Health data tracked on phones and devices is one way medicine can become more personal, you argue.

There are quite a number of devices for measuring blood pressure, heart rhythm, and blood glucose on a continuous basis. I can do a complete ultrasound of the body in high resolution with my smartphone, during [a] physical exam. You don't have to send nearly as many patients for the $800 to $1,000 ultrasound test, and you

SILICON VALLEY BANK; JOE CIARDIELLO

can share it with the patient during the exam. With smartphones you can do an ear exam on a child, or an eye exam without an eye doctor, you can measure Parkinson's tremor, voice, and gait and know whether you should take your medicine and at what dose. We're heading toward being able to do your own medical selfie. Most people judge [self-monitoring] by things like Fitbit and step counting, and that's so off base.

With smartphones you can do an ear exam on a child, or an eye exam without an eye doctor.

As you point out, mobile advances have coincided with increased use of a very different technology, genomic medicine.
There has been a remarkable drop in the cost of genome sequencing. The problem we have right now is a lot of these new drugs [being developed based on genomic analysis] are for rare conditions and are off-the-chart expensive. If you can achieve a cure with genome editing, then the question is what should that cost? What would it be worth to get a cure via gene editing instead of going through a perpetual, very expensive treatment with risks and side effects?

You are a proponent, but does anything concern you about this new medicine?
The biggest disappointment is security. Our medical data is being sold, hacked, breached. Over 100 million Americans have had their [medical] records hacked in the last year, versus maybe five million that have accessed their records online. That's the vulnerability.

People don't own their medical data, and they rightfully should. They are generating an ever increasing amount of data through their own devices. There's no home for that data. There's tremendous resistance from the medical community, but we need to embrace this shift in power to the patient.

Is it hard to make sense of so much data?
That's the next problem, handling the data and processing it using artificial intelligence and deep learning. We are not nearly as far along as we should be. This is a bottleneck that can only move forward when the data is getting processed in real time with feedback to the individual by validated algorithms. Companies are working on this. The idea is to capture all this data (such as from sensors and imaging), enabling machine learning and predictive analytics, and giving individualized guidance based on that.

How long do you think it will be until that challenge is solved?
I am always unrealistic, hoping for things to change quickly. This will take time.

Case Study

A Big Bet That Gene Editing Will Cure Human Disease

Raising millions, Editas proved that investors are enthusiastic about gene editing. Now the company has to make its technology work.

● Huddled with Wall Street investment bankers outside a hotel ballroom in downtown New York last January, Katrine Bosley was getting some sobering news. The stock market, falling since early December, was continuing to dive, with her industry, biotechnology, especially hard hit. The previous year had been the worst for new stock offerings in the history of the tech-heavy Nasdaq, and now Bosley had to persuade the roomful of investors lunching on the other side of the wall that her company, Editas Medicine, could break the trend.

Editas specializes in a process called gene editing using a technology known as CRISPR/Cas9. Because this technology makes it possible to edit DNA precisely and more easily than earlier methods, it has quickly become popular with scientists in the four years since it was first described. Editas was cofounded by several of the early developers of CRISPR. Now it aims to find ways to transform this tool into a method of treating genetic diseases that for the most part have no treatments today. Editas is researching therapies aimed at eye disease, cancer, sickle-cell anemia, and Duchenne muscular dystrophy, among others.

Outside scientific circles, CRISPR is still far from widely understood, and Bosley had spent much of her time since joining Editas in June 2014 pitching venture capitalists and possible investors on its potential. Even so, the investors in that New York hotel had plenty of questions about the company—and some remain even after Editas's highly successful initial public offering, which raised $109 million in February.

The company has no revenue from product sales and expects none in the foreseeable future. It has more than $200 million in cash, enough to last two years, but must in that time create a product unlike any that has ever existed before. It won't begin to test its treatments on humans until sometime next year. Even if that is a success, it is unclear when they will be commercialized.

What Editas has going for it—besides Bosley and a premier group of scientific founders—is the potential for gene editing to fundamentally change medicine.

"It's such a powerful tool," says Jim Flynn, managing director of Deerfield Management, which runs $5 billion in health-care investments, including a stake in Editas. "There are people here who believe that when we look back in 10 years we will see a demarcation: before gene editing and after."

Editas cofounders George Church and Feng Zhang were the first to show that CRISPR could work with human

cells. Hoping to exploit the technology's commercial possibilities, a trio of health-focused venture firms in the Boston area convinced Church, Zhang, and others to form Editas only months after their papers were published in scientific journals. Editas isn't the only company looking to develop gene-editing treatments. Rival Intellia Therapeutics, with which Editas is involved in a patent dispute, went public just three months after Editas. Last December, Bayer agreed to invest $335 million in a joint venture with yet another company, CRISPR Therapeutics.

Bosley has said Editas will be far enough along to begin testing in humans next year. The plan is to inject a virus containing Cas9 into the eyes of people suffering from a rare form of progressive blindness caused by a specific gene mutation. The enzyme would then cut the faulty sequence, triggering a natural DNA response in which the cell repairs the deficit itself. Starting with this eye disease has some advantages, because its genetic basis is clearly understood and the treatment can be delivered locally to a target.

Still, significant technological challenges remain. Editas must make an effective treatment, ensure it can reach the site of the disease safely, and edit the DNA properly—all without dangerous side effects.

The company also has to hope that ethical questions about some potential uses of CRISPR do not cloud the technology and delay regulatory approval. For example, some scientists are concerned that the technology could be used to engineer human embryos. Though this is not something Editas is working on, Bosley has met with groups from French members of Parliament to U.K. bioethicists to discuss that and other topics.

She says the best advocates for the technology are patients with the untreatable genetic diseases Editas hopes to address. For them, effective gene editing could be a crucial medical breakthrough. Now Bosley has to prove that Editas can develop something that fits that description. *—Nanette Byrnes*

Timeline

Precision Medicine Pioneer

Herceptin, the original genetic drug, showed that not all cancers are alike.

● Herceptin is the original targeted drug therapy. The medication, which targets the HER2 protein associated with an aggressive form of breast cancer, was developed by the biotech company Genentech and won approval from the U.S. Food and Drug Administration in 1998. It has been used to treat more than two million patients worldwide and has generated global sales of more than $64 billion for the Swiss pharma giant Roche, which owns Genentech and markets Herceptin outside the U.S. Here's how the pioneer of precision medicine has evolved. *—Elizabeth Woyke*

1985
National Institutes of Health shows that *HER2* gene is frequently amplified in human breast tumor cells.

1990
Genentech scientists, having cloned the first human *HER2* gene earlier, create Herceptin by humanizing a mouse antibody directed at *HER2*. Third parties later estimate Genentech's development costs to be $150 to $200 million.

1992
Genentech requests authorization from the FDA to administer Herceptin as an investigational drug.

1992–1998
Clinical trials look at the safety and efficacy of Herceptin alone or with chemotherapy for people with *HER2*-positive metastatic breast cancer.

March 1998
Genentech announces collaboration with diagnostics company Dako to develop commercial test to identify patients who overexpress *HER2*.

May 1998
Genentech requests FDA permission to market Herceptin. FDA designates it a "Fast Track" and "Priority Review" product, which means it fills an unmet medical need for a serious condition and will be reviewed within six months rather than the standard 10.

September 1998
FDA approves Herceptin for the treatment of *HER2*-positive metastatic breast cancer and approves a diagnostic test to help identify patients.

August 2000
First European approval.

2006–2008
FDA approves three different Herceptin-based regimens for post-surgery treatment of early-stage *HER2*-positive breast cancer. Approval for gastric cancer follows.

2014
First patent for Herceptin expires in Europe. Following the lead of an Indian biotech firm that got a highly similar version of the drug approved in 2013, a South Korean company receives approval for a "biosimilar" that shows no clinically meaningful difference in safety or effectiveness from the original product. Other Asian approvals follow.

May 2015
Shortly after President Obama announces his $215 million research project on precision medicine, the World Health Organization adds Herceptin to its list of essential medicines for low- and middle-income countries.

2019
First patent for Herceptin is scheduled to expire in the U.S.

SOURCE FOR TIMELINE: THE $800 MILLION PILL: THE TRUTH BEHIND THE COST OF NEW DRUGS, COMPANY REPORTS

Profile

Craig Venter's Latest Production

With more data, a pioneer of gene sequencing hopes to unlock the connections between DNA and illness.

REBECCA CLARKE

● At Human Longevity Inc. (HLI) in La Jolla, California, more than two dozen machines work around the clock, sequencing one human genome every 15 minutes at a cost of under $2,000 per genome. The whole operation fits comfortably in three rooms. Back in 2000, when its founder, J. Craig Venter, first sequenced a human genome (his own), it cost $100 million and took a building-size, $50 million computer nine months to complete.

Venter's goal is to sequence at least one million genomes, something that seems likely to take the better part of a decade, and use the data generated from them—along with information about some of the DNA donors' health histories and the results of other medical tests—to find better ways to treat and prevent a range of disorders common among aging people, from cancer to heart disease.

Venter, 69, has raised $300 million from investors that include GE Ventures, the biotech company Celgene, and Illumina, which supplies the sequencing machines. And HLI has partnerships with the British pharmaceutical giant AstraZeneca and the South San Francisco–based Roche subsidiary Genentech, both of which are contributing patient samples for sequencing.

Seated behind his desk in his office two floors above the sequencing lab, his red poodle Darwin sleeping quietly at his feet, Venter has pulled up images on his computer that show how in one early experiment HLI scientists were able to sequence 1,000 people's genomes and then reconstruct their faces solely on the basis of the genetic data. "We can predict your face, your height, your body mass index, your eye color, your hair color and texture," he says, marveling at how closely one of the reconstructed faces matches the photo of the actual study participant.

But Venter says the ability to make faces out of genomes only hints at the full power of genetics. "Whether it's the shape of your face, or a [diseased] aorta, or a narrowing of your spinal cord, we want to measure it so we can be able to predict those conditions in the future from the genetic code," he says.

The understanding of genomics is still in its infancy, limiting the ability to draw firm links between genes and diseases. Even genes that have been well characterized don't always lead researchers to medical breakthroughs. For example, Venter discovered he has a favorable variant in a gene called *CETP* (cholesteryl ester transfer protein) that had previously been associated with naturally healthy cholesterol levels and, by extension, a lower risk of heart attacks and strokes. In the early 2000s several pharmaceutical companies tried developing drugs to lower bad cholesterol levels by targeting a deleterious variant of the gene that leads to high levels of unhealthy cholesterol. They all failed.

"What that proves is that simple correlations don't always work out. The whole field is learning there is complexity with this," he says.

Venter is embracing the complexity, arguing that combining genomic information with other health data will unlock those links. Under the arrangement with AstraZeneca, the drug company will share 500,000 anonymous DNA samples from patients in its clinical trials with HLI, which will sequence and analyze the patients' DNA. "Technology allows us to read every single letter of the genome, but the ability to detect sequence differences between hundreds of thousands of patients will make a huge impact in understanding both disease and drug response," says Ruth March, who heads the pharma company's initiative on personalized medicine and biomarkers. "HLI

$300 million
Venture capital invested in Venter's Human Longevity Inc.

has the technology to spot patterns in data and build upon them, rather than just looking at random genes."

To understand the health significance of each of the 20,000 or so genes in the human genome, scientists need to compare the genetic data with other information about the same people: data revealing how their genes are affected by environmental factors and behavior, records showing how they have responded to drugs, MRI images and other results from medical tests, and more. Only by discovering patterns among those data points, Venter believes, will HLI gain insights that physicians can use to practice precision medicine, tailoring treatment choices to the exact genetic makeup of each patient.

Correlating petabytes of genetic data with specific health conditions and then scanning for patterns among the million individuals whose genomes HLI is collecting is an enormous computing challenge. So Venter hired Franz Och, Google's former machine-translation chief, who is best known for leading the development of Google Translate, software that translates any website in the world into English almost instantaneously.

The challenge, says Och, is to correlate health conditions to the 6.4 billion letters that make up the genetic code. That code can be thought of as one language, MRI images as another language, and so forth.

The technology might be used in people with Alzheimer's, whose hippocampi often shrink years before they develop symptoms. Using machine learning to compare full genomes with brain images could uncover genetic variations that are related to Alzheimer's risk. That might then yield targets for new drugs or early-detection devices. Or, says Och, it could reveal why some people with certain known genetic risk factors don't get sick. "There might be other genetic changes that are protective," he says.

One of HLI's goals is to make cancer vaccines that are tailored to patients' genetic makeup and their particular cancer. The idea would be to treat patients first, sequence their tumors as well as their entire genomes, and then give them a vaccine that would prevent their disease from returning, says Ken Bloom, president of HLI and head of its oncology initiative. "It would prime the immune system and prepare it for another assault by the cancer, so it won't recur," Bloom explains.

Venter envisions a day when all of us will be able to have our genomes sequenced and used to improve our health care. He launched a prototype of that model in October 2015, called the Health Nucleus. Patients spend a day at the company's La Jolla headquarters, getting their genome sequenced and undergoing medical tests. Health Nucleus customers, who pay $25,000 for the service, start their day in a private suite, decked out with leather chairs, discussing their family histories with a staff doctor for 90 minutes and having blood samples taken. Then they're put through a battery of high-tech imaging tests that aren't usually prescribed for healthy people, such as full-body MRI scans and 4-D echocardiography, which takes time-stamped pictures reflecting the full shape of the heart over time. They go home with a Band-Aid-size device on their chest that measures their heart rhythms for two weeks. All customers get access to a mobile app, where they can click on a 3-D avatar of themselves to learn which of their genes correlate to potential health conditions that might affect their heart, brain, and other vital organs. About 220 patients have signed up so far.

"Whether it's the shape of your face ... or a narrowing of your spinal cord, we want to measure it so we can predict those conditions."

That approach has brought up a host of ethical and societal quandaries, says Arthur Caplan, a professor of bioethics at New York University's Langone Medical Center, who has known Venter for many years and once worked as an advisor on one of his ventures. Who is going to pay for all this testing and personalized medicine? Is it even worth the money? Caplan points out that anybody who wants genome sequencing today has to pay out of pocket, because insurance companies rarely reimburse patients for genetic testing or counseling. So for now, at least, there's an economic disparity in access to these highly tailored health regimens. "It's only the rich who can pay right now for genome sequencing," says Caplan.

That might be true for now, but Venter has hired actuaries to help prove out the economics of HLI's personalized approach, hoping to get insurance companies on board. Even if it costs $25,000 per patient, he says, it beats spending hundreds of thousands of dollars on chemotherapy and other treatments that ultimately won't save lives. "So $25,000 vs. hundreds of thousands of dollars, 40 years left to live vs. two years left to live," he says. "How many of those cases do you need to say it's more economical to prevent disease rather than just to treat it?"

—Arlene Weintraub

Case Study

Taking Genomic Data Global

Startups focused on Asia are among those aiming to bring precision medicine to far more people.

● Colon cancer is less common in India than in the U.S., but it tends to affect younger people and to be more aggressive when it does occur there. Indians with colon cancer also have different genetic mutations from the ones affecting patients who have been studied in Western countries and whose information is the basis of most published data on the disease. A vegetarian diet may help explain the overall statistics, but why do some Indians develop a more serious form of the disease at a younger age?

Doctors suspect that differences in the genome may help explain how colon can-

cer expresses itself in the two groups. A startup called Global Gene Corp plans to study Indian patients' genomes to find links to cancer and whether these yield clues to better treatment.

The company will analyze patients' DNA as well as the genomics of their cancer cells, using algorithms to identify treatment options for individuals—as well as broader trends. Aggregate data could be relevant for pharmaceutical companies looking to develop new medicines, and for policy makers, too.

Examining genetic patterns, Global Gene Corp hopes to gain insight into cancers and other ailments that affect Indians.

Global Gene Corp thinks that by examining genetic patterns, it can help uncover important insights into a number of ailments that affect Indians, among them diabetes, a type of liver disease called Wilson's disease, and multiple cancers. It offers tests to make diagnoses, to predict whether a person is a carrier for or has an inherited disposition to a disease, and to determine the best type or dose of medicine for an individual.

Among the genetic mysteries the company hopes to solve is why Indians are predisposed to diabetes and other obesity-related diseases at a lower body mass index than Westerners.

The firm, which is based in Singapore, got its start in Boston in 2013, when two Harvard Medical School physicians joined two executives to explore how to use genomics to improve health care in the developing world. The quest took them to India, which despite its huge population and rich diversity has largely been left out of the explosion of genomic information that followed the first sequencing of a human genome in 2003. According to the company, just 0.2 percent of genomic data comes from India, even though it has 20 percent of the world's population.

The situation is similar across much of the world. Though countries outside the U.S., Europe, and Japan make up 60 percent of the world's population, they contribute less than 1 percent of sequenced genomic data globally, the company says.

This is largely because poor countries historically focused their health resources on managing and eradicating communicable diseases and did not establish programs like the Human Genome Project in the U.S. and Genomics England in the U.K.

Global Gene sees a business opportunity in this omission. Taking into account population predictions, cancer statistics, and pharmaceutical research spending, company executives think the Indian market for genomic information that could be used in drug development and cancer treatment may reach $1.9 billion. Adding in China, Southeast Asia, and the Middle East—areas where Global Gene hopes to expand—would increase the total addressable market to $8.1 billion, with a 14 percent annual growth rate, according to the company.

The closely held company won't disclose its revenue, but it has raised private investor funding and forged partnerships with 48 business, government, and scientific organizations across Asia and Europe. The Wellcome Trust Sanger Institute, which played an important role in the original sequencing of the human genome, now houses Global Gene's R&D center on its campus in Cambridge, England.

The company has also already gathered more than 10,000 DNA samples with patient consent, resulting in what it says is India's largest genomics biobank, and established the core for a reference genome (a digital "average" genome) for Indians. It says a reference genome will help it derive insights about the many diseases in India.

Global Gene isn't the only player with its eye on Asia. A nonprofit consortium of academics and companies, called GenomeAsia 100K, wants to sequence 100,000 people in South, North, and East Asia and create perhaps 50 to 100 reference genomes, representing all major Asian ethnic groups, within the next four years. Japan, for example, is believed to have three major ethnic groups, with some degree of genome variation, according to project leader Stephan Schuster, a biology professor who is research director of the Singapore Centre on Environmental Life Sciences Engineering at Singapore's Nanyang Technological University.

Why study Indian genomes?

Indians derived from two populations of origin that branched thousands of years ago, and are distinct from other populations, according to Global Gene Corp. This means the vast majority of Indians share commonalities, and that one Indian ethnic group's predisposition to a certain disease can be more clearly understood by comparing the genetics of that group against the rest of the Indian population. As a result, creating a reference genome for Indians—and other Asian populations—will help yield insights about managing disease, treating individuals, and developing therapies.

JOOHEE YOON

Previous attempts to document human genetic variation failed to shed much light in South Asia. The 1000 Genomes Project, which ran between 2008 and 2015 and was designed to capture population diversity, sequenced genomes from only a few South Asian ethnic groups, among them Gujarati Indians and Pakistani Punjabis. An earlier, smaller effort called the International HapMap Project, which was supposed to be a catalogue of common human genetic variants, gathered DNA from just one South Asian population (Gujarati Indians).

Government-funded genome projects may yield more information. Genomics England's 100,000 Genomes Project, which is sequencing patients who have rare diseases and cancer, records participants' ethnicities and considers how that information may be relevant to the patient's condition. In the United States, President Obama's Precision Medicine Initiative Cohort Program, which is set to launch later this year, will collect participants' ethnicity, amongst other data. Its goal is for this data to help researchers study individual differences in health and disease.

Such large-scale genetic mapping projects have often struggled to acquire enough samples to draw meaningful conclusions. Global Gene is trying to sidestep the problem by obtaining samples through multiple sources, including partner hospitals, research projects, and voluntary donations from individuals who arrange for testing on their own.

Payment may be an issue, says Lawton R. Burns, a professor of healthcare management at the University of Pennsylvania's Wharton School who has written books about China and India. He estimates that only 25 percent of Indians have medical insurance, and most of those plans wouldn't cover genetic testing. "To make this work, you need people who not only want to know their genetic makeup but are engaged in their health care, have the money to pay for the test, and are willing to spend that money," Burns says.

Global Gene's clinical tests range in cost from $75 to $538. India's median income was $616 in 2013, according to a Gallup survey.

And there is another big problem, Burns says: "Even if patients buy the tests, what will they be able to do with the information?"

Global Gene is trying to make the tests useful. Many of the startup's genetic tests incorporate a proprietary technology that recognizes mutations commonly seen in Indians. Insights from this multigene assay provide a baseline that helps the company differentiate clinically insignificant genetic variations present in the Indian population from potentially pathogenic ones.

Using this, plus its software, it can gauge whether a person is likely to suffer potentially life-threatening complications from taking cholesterol-lowering medications known as statins. It can also screen for mutations in genes that are known to increase cancer risk, such as *BRCA1* and *BRCA2*, which are linked to a much higher chance of developing breast and ovarian cancer. (Indians and Western populations have different groupings of *BRCA* mutations.)

Data from the tests can be used to identify people with particular genetic characteristics, whom pharmaceutical companies could recruit to expedite drug trials.

"To change health, we have to represent the world," says Jonathan Picker, a Global Gene cofounder who is also a geneticist at Harvard Medical School. "It doesn't make sense to take a couple of subsets and assume that now we understand everybody." *—Elizabeth Woyke*

TRANSCEIVERS SPEED DEVELOPMENT OF NEW MILITARY AND FIRST-RESPONDER COMMUNICATION SOLUTIONS

Police, fire, and emergency medical personnel arrive at a small tornado-ravaged town. U.S. Special Forces, unmanned aerial vehicles, and naval vessels are deployed halfway around the world. In both scenarios, communication is vital but often impeded by the different devices these groups use, which don't always interoperate.

Software-defined radio (SDR) solves that problem by making it possible to rapidly define a device's application using software-programmable capability. That capability potentially saves lives during battles, natural disasters, and other crises by enabling key personnel to share vital information in real time. By replacing special-purpose radio equipment, programmable radio-frequency (RF) transceivers can limit the need for additional hardware while accelerating new product development for those situations and many others.

However, with 100 billion connected devices in use worldwide and spectrum availability becoming scarce and congested, RF component manufacturers are under pressure to build high-performance systems that operate robustly in many different scenarios.

RF Transceivers and Development Tools Can Fuel or Hinder Innovation

Among the biggest challenges facing solution providers is reducing weight and size while adding more features to new devices and improving their performance.

For example, soldiers need mobile devices that allow them to communicate seamlessly, reliably, securely, and in real time over varying terrains, while supporting different frequencies and bandwidths via various airborne, satellite, and terrestrial links.

Radio manufacturers have nominally solved this problem by purchasing and cobbling together several discrete components from multiple chip vendors to build new mobile devices.

While that approach meets some of the military's demands, using so many different components reduces battery life and increases the size and weight of soldiers' communications packs.

"The number of discrete components and band-specific filters also slows development time," explains Kim Boucher, marketing director for radio transceivers at Analog Devices, Inc. (ADI). "It's a direct hit to R&D efficiency."

Some devices contain 20 or more components, Boucher adds, which can inflate and fracture product teams—forcing engineers to focus on discrete elements rather than having a unified vision of the end product. Using several designs also makes it difficult to create prototypes and identify the sources of technical problems, compromising quality control and limiting innovation opportunities. Multiple components add administrative overhead for inventory control, supply management, and procurement, Boucher says.

RadioVerse gives radio communication providers the technology and tools needed to make a difference for military personnel, first responders, and others who save and protect lives.

RadioVerse Development Platform and Ecosystem

Recently, ADI launched both its new 12mm x 12mm AD9371 transceiver and RadioVerse, a development platform and ecosystem. Together, these solutions enable product developers to dramatically streamline time to market. The AD9371, which features a 300-MHz to 6-GHz frequency range, “is frequency-band agnostic and reduces the number of components needed from as many as 20 to 1,” Boucher says.

In addition, solution providers don’t have to redesign their products or add multiple components to support different frequencies or bandwidths because that capability is built into the AD9371.

“It’s capable of scanning a wide frequency range and is easy to implement, allowing solutions vendors to eliminate many of the hardware components they have used in the past,” Boucher says.

Instead, vendors can develop their new products in software and thus have more time to fine-tune them using RadioVerse’s common-design platform, including prototyping tools that support multiple applications and standards. “RadioVerse allows engineers to try out ‘what-if’ simulations in software,” Boucher says.

In addition to speeding up product development, the AD9371’s programmability also allows easy customization and upgrades. The transceiver’s size and weight also allow myriad new applications such as multi-band base stations and systems mounted on buildings, light poles, and office walls, as well as long-range high-definition video links from unmanned terrestrial and aerial vehicles. The compact, low-power, rugged AD9371 can also support massive antenna array applications. Such a system built with multiple components would be problematic due to weight, size, and coverage limitations, Boucher explains.

RadioVerse and the AD9371 help address another common problem.

“It’s increasingly difficult to recruit hardware engineers with RF expertise. Meanwhile, a growing number of software engineers are graduating every year,” Boucher says. “RadioVerse provides a software-based development platform that minimizes the need for deep RF hardware expertise. It’s easy to use and learn, and is a great environment for software and system engineers to develop their products.”

The military and other communication-infrastructure markets are under pressure to optimize mobile voice and data services, Boucher says: “Our common development platform supports flexible product design, rapid prototyping, and innovation, making users of the RadioVerse platform compete more effectively in the market.”

Choosing the Right Technology Partner

To meet and exceed customers’ demands, solution developers must choose technology partners carefully. Some chip manufacturers are moving beyond simply providing components and becoming inventors and collaborators. In this role, manufacturers can be ideal technology partners by anticipating market shifts (for example, moving from hardware- to software-based engineering) and providing deep knowledge about the requirements and demands of vertical markets. The best technology partner works closely with product teams to offer the long view, understand end-user needs, and avoid dead-end designs.

In Boucher’s opinion, that kind of approach gives birth to innovations such as RadioVerse and gives radio providers the tools needed to make a difference for military personnel, first responders, and others who save and protect lives.

For more information, visit **www.analog.com/radioverse**.

Reviews

DANIEL ZENDER

Can We Help the Losers in Climate Change?

The demise of the coal industry should start a discussion of how we will respond to the economic upheaval caused by global warming.

By Richard Martin

The coal industry in the United States has been in a long, steady decline for decades. But since 2012, with the availability of cheap natural gas and the ramping up of environmental regulations to control emissions from coal-fired power plants, that decline has become a full-scale collapse: coal-mining employment has shrunk from 89,800 to 55,500, a drop of 38 percent, according to the Bureau of Labor Statistics. And though the coal business is no stranger to boom-and-bust cycles, this is something different. Emissions limits are becoming ever tighter under regulations such as the federal Clean Power Plan, and the utility industry is looking for more sustainable sources of power. Those jobs are never coming back.

The losses have been concentrated in Appalachia, once America's coal heartland. Coal-mining counties in southern West Virginia and eastern Kentucky have rates of unemployment twice the national average, and in some areas the real jobless rate—including people who have effectively exited the workforce—reaches nearly 50 percent, according to local officials.

But it would be a mistake to dismiss the problem as a regional one uniquely related to the slowing demand for coal. In many ways, the disappearance of the coal economy is a harbinger of major transformations that climate change will bring about in other regions and other sectors. Industries from agriculture to real estate are likely to be devastated by global warming. While the effects on those sectors will look very different from the impact on the coal industry, the results will be similar: economic harm to large regions of the country. And yet little thought has been given to comprehensive, fair, effective strategies to manage those disruptions. In that sense the demise of the coal industry in West Virginia and Kentucky is just a trial run for much larger challenges ahead.

"What happened here happened so quickly, I don't think anyone was prepared," says Donovan Beckett, a physician who founded a free clinic called the Williamson Health and Wellness Center in his West Virginia hometown. "I don't know if anyone has come up with a solution that's really going to help."

Dust bowls

There is a growing body of literature on the likely economic consequences of climate change, but far less research has been done on how to ameliorate those effects for workers and communities. *Economic Risks of Climate Change*, by a team of researchers headed by Robert Kopp, a

President Obama's Power Plus Plan
February 2015

Economic Risks of Climate Change
Trevor Houser, Solomon Hsiang, Robert Kopp, and Kate Larsen
Columbia University Press
August 2015

climate scientist at Rutgers, and Solomon Hsiang, a professor of public policy at the University of California, Berkeley, finds that among the regions most affected by climate change will be the coasts: by 2050, losses of property due to the rise in sea level will total between $66 billion and $106 billion, they estimate. States such as Iowa and Nebraska, which depend heavily on farm crops vulnerable to rising temperatures and more severe droughts, could see annual per capita income decline nearly $2,000 by the end of this century. (Some states could benefit from longer growing seasons: per capita income in North Dakota, the authors find, could rise by more than $2,500 a year.)

One economic effect of climate change will be on labor productivity, particularly for workers who toil outdoors or in environments significantly affected by hotter temperatures. Kopp and Hsiang identify four high-risk sectors—agriculture, construction, utilities, and manufacturing—that together account for about a quarter of the U.S. labor force and just under one-fifth of GDP. States that depend heavily on these sectors, such as Louisiana, Indiana, and Iowa, could be hardest hit by declines in labor productivity. Nationwide, the authors forecast, the total cost of productivity impacts will be between $42 billion and $150 billion by 2100.

No sector will be affected more than agriculture. In 2015 alone, the California drought cost the economy $2.7 billion and eliminated some 21,000 jobs, according to the Center for Watershed Sciences at the University of California, Davis. In *Economic Risks of Climate Change*, Hsiang and his colleagues found that parts of the U.S. Midwest, Southeast, and Great Plains—some of the most fertile farmland in the country—could see annual crop yields fall 20 to 50 percent by midcentury. “When you look at regions that we consider heavily impacted by the Dust Bowl, we saw agricultural declines of 15 percent,” says Hsiang. “What we’re saying is that according to our projections, there’s a 50 percent chance that we’ll see what looks like a perpetual Dust Bowl situation.” The number of agricultural workers in the U.S. is expected to drop 6 percent from 2014 to 2024 even *without* accounting for climate change. Its effects could easily increase that to more than 10 percent.

There are going to be far fewer people building and selling coastal property in North Carolina, growing cotton in Arizona, and working drilling rigs in North Dakota in the coming decades. How will we help them find other livelihoods?

Moving on

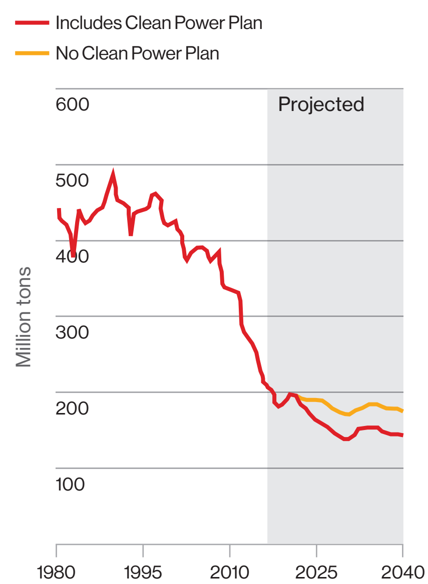
As part of its 2017 budget plan, the Obama administration proposed a program to help the distressed communities of Appalachia and other coal-dependent regions make the transition from mining to more sustainable economies. Obama’s Power Plus Plan includes $75 million for job retraining and economic diversification, most of that in competitive grants to communities and nonprofits. It would shore up pension and health-care funds for retired coalfield workers whose employers have shed their pension obligations, and it would free up $1 billion from the Abandoned Mine Reclamation Fund to reclaim old mine sites, clean them up, and redevelop them as industrial parks and economic development zones. Hillary Clinton, who was harshly criticized in March for her remarks on shutting down coal mines, has produced a $30 billion plan to revitalize communities threatened by coal’s decline. It includes many of the same features as Obama’s, at wider scope.

Unfortunately, even $30 billion may not be equal to the challenge. Both of these schemes are based on ideas that will sound familiar to anyone who has followed previous federal efforts to bring prosperity to Appalachia. Central to all of them is job retraining. Many coal miners, the thinking goes, have mechanical skills that can easily be transferred to deployment of new energy systems—installing solar panels, for instance. “There’s going to be way more jobs in the renewable distributed energy system,” says Jennie Stephens, a professor of sustainability science and policy at Northeastern University. “We should be focused on helping people embrace the new opportunities these transitions will bring.”

Research on job retraining, though, shows that the results are mixed, at best. A 2008 Department of Labor study that looked at retraining programs involving 160,000 laid-off workers in 12 states concluded, “It appears possible that ultimate gains from participation are small or nonexistent.” A more recent study from the Hamilton Project found that to be successful, retraining programs must be highly targeted at the workers most likely to benefit. In general, that means younger

Appalachia Coal Production

The Clean Power Plan stands to hurt coal mining somewhat, but the industry is already doomed.



DATA FROM EIA

workers with some postsecondary education who are motivated to follow through, and who are able and willing to relocate to places with more job opportunities. Many of the unemployed coal miners of Appalachia do not fit those criteria.

We need to shift away from piecemeal plans. We need a comprehensive effort to reshape regional economies.

The idea that many people should just get out of Appalachia has been around for decades. "Economic betterment for the great majority of the people of the Southern Appalachians is not to be found in development of the meager resources of the local area," wrote economists B. H. Luebke and John Fraser Hart in 1958, "but in migration to other areas more richly endowed by nature and by man." In economic theory, human mobility should benefit both the downtrodden areas people are leaving, by tightening the job market, and the more prosperous ones that need new workers. Subsidizing migration, though, has moral and political implications that many find unsettling. "There's a psychic cost to relocating—if there weren't, we'd see a lot more mobility in the U.S. than we do," says Reed Walker, an assistant professor at the Haas School of Business at UC Berkeley.

Ultimately, though, it will be necessary to address the costs of rejuvenating communities affected by climate change. Some workers can be retrained, but some can't. Some towns can recast themselves with music festivals and art fairs, but not all. Crafting solutions requires a level of forethought, planning, and clear-eyed decision-making that our institutions and elected officials have not shown themselves to be particularly good at. Few officials have even acknowledged the scale of the challenges ahead.

"These answers have to be carefully thought out, and serious strategic work needs to be done, before you start handing out money," says Amy Glasmeier, a professor of economic geography and regional planning at MIT who worked for many years at the Appalachian Regional Commission. "We have to figure out the problem first, and understand the demographics and the politics and the return on investment, and then launch programs—instead of saying 'We've got to spend money now, because next year we'll have to ask for more.'"

Given that such questions could soon be relevant far beyond coal communities, we will need to shift away from piecemeal, short-term, narrowly focused retraining efforts that attempt to quickly plug workers into new jobs. Instead, we need a comprehensive effort to reshape regional economies. President Obama's proposal to devote $60 billion to making community colleges free for all qualified students, and to expand vocational training and apprenticeships for jobs in expanding fields, could be one way to start.

For the coal miners of Appalachia, such efforts could offer a chance to move beyond an extractive industry that for decades brought jobs, but not prosperity, to the region. "There is too much focus right now on 'How do we replace these 10,000 good-paying jobs for people with only a high school diploma?'" says Peter Hille, the president of the Mountain Association for Community Economic Development in Berea, Kentucky. "That's not the right question. The real question is 'What can we do to create a new, diverse, and sustainable economy in a region that's been economically distressed for more than a half-century?'"

Richard Martin is senior editor for energy at MIT Technology Review.

JORDAN SPEER

The Next Must-Have Smartphone Feature

Google's new location-sensing system will make augmented reality far more useful.

By Elizabeth Woyke

Smartphones can tell you when to depart for the airport to make your flight, provide voice-guided directions on the way there, and route around traffic jams. But if you wanted to get audio directions to a specific counter at the airport, you'd be out of luck. That requires a phone to understand its position in great detail, all on its own—even when it is deep inside a building, beyond the reach of GPS signals. Even the most sophisticated phones can't do that.

That has long frustrated Google engineer Johnny Lee. Why should he "give up on using my cell phone," he says, when try-

Tango
Google

Phab2 Pro
$499
Lenovo

Dinosaurs Among Us
American Museum of Natural History

Lowe's Vision
Lowe's

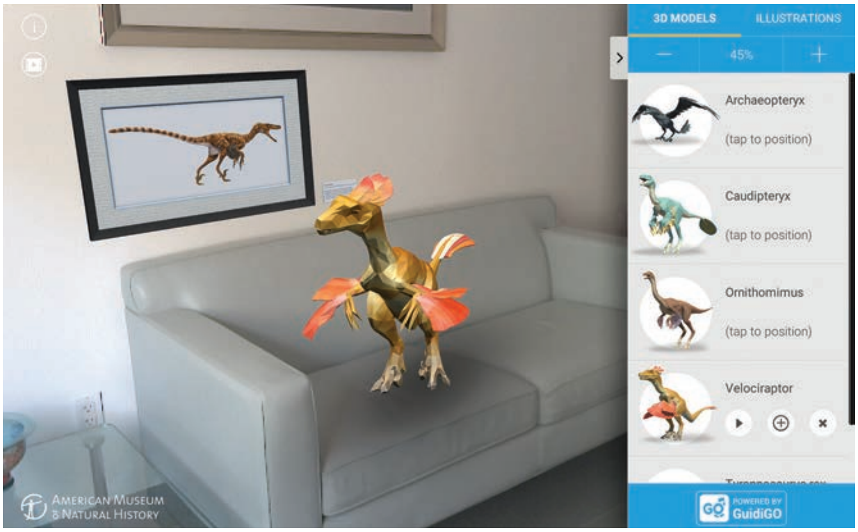
Phantogeist
Trixi Studios

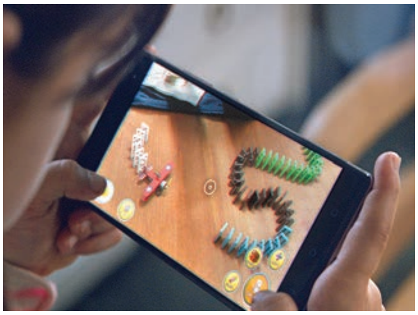
WayfairView
Wayfair

ing to find things inside large buildings? When I talked to him, he was traveling in Singapore, where he had been visiting big malls—and getting lost. As soon as he walked through the front door, he said, his phone had become "somewhat useless."

But thanks to Tango, a location-sensing system that Lee is developing at Google, phones are about to get much more useful—especially when they're indoors. In the works for nearly four years, Tango uses sensors, computer vision, and image processing to give phones a much better comprehension of space and motion. It is built on three core technologies: area learning, depth sensing, and motion tracking. Together, they allow Tango phones to learn, remember, and map areas around them; detect how far they are from the floor or a wall or an object; and understand where they are while moving in three-dimensional space. Tango can do this with centimeter-level accuracy, all without relying on external signals such as GPS, Wi-Fi, or Bluetooth.

And because Tango makes devices so adept at understanding their position, it's much more than the equivalent of indoor GPS. It will let phones interact with their surroundings or with virtual objects in novel ways. If you're shopping for a new sofa, Tango-enabled apps from Lowe's and Wayfair will show you which styles will fit the space available and let you plop 3-D images into your living room to see how they would look. Need to measure a painting so you can frame it, or get the dimensions of a bureau so you can sell it online? Tango can use tracking and 3-D sensing data to calculate the dimensions of objects, no ruler or measuring tape needed. Bored? Fire up Phantogeist, a





Top: The American Museum of Natural History's augmented-reality app about dinosaurs. Bottom: A Wayfair furniture app and an AR domino game.

Tango game in which phantom-like aliens lunge at you from behind walls and under floors. Or launch Dinosaurs Among Us, an app from the American Museum of Natural History that relies on Tango. It lets you place dinosaurs around your house and see facts derived from the museum's current dinosaur exhibit.

Compare that with Pokémon Go, which caused a craze on smartphones this summer even though its characters didn't really interact with their environment in a realistic way. If Pokémon Go were on Tango, players would be able to approach the cartoon creatures and circle around them instead of just looking at them straight on, from a distance. The characters would appear larger when in close proximity and could be viewed from multiple angles. They would seem to be part of the landscape rather than hovering in the air.

Tango's greater powers will lead to entirely new kinds of augmented-reality applications, says Blair MacIntyre, director of the Augmented Environments Lab at Georgia Tech. "Being able to scan the world on a smartphone opens up all types of possibilities, including apps that do things we researchers have only demonstrated in our labs, using really expensive equipment," he says.

Lenovo will release the first Tango device for consumers—a $499 Android smartphone called the Phab2 Pro—this winter. It comes at a time when we are figuring out the best ways to merge the virtual world with the real one. Of the many potential paths forward, Tango stands out for its wide range of functions and ease of use. This thing you probably haven't heard of has a good chance of being the next must-have smartphone feature.

Helping devices see

Mobile AR apps have been available for years, but Tango is more advanced because it understands its surroundings rather than simply overlaying images on them. GuidiGO, a French-American startup that makes mobile-device-based guided tours for cultural and historical sites, has been testing Tango to produce phone and tablet tours for museums. The apps direct visitors to particular objects by displaying a path of virtual blue dots on top of the floor. When visitors arrive at a featured work, they see a virtual button that appears to be hovering in the air. Touching that virtual button brings up images that appear like a special effect in a movie. In an ancient Egyptian gallery, it could be an x-ray view of a mummy's sarcophagus. GuidiGO also makes apps for regular Android phones and tablets, iPhones, and iPads, but cofounder and CEO David Lerman says the company's Tango-based tours are the most immersive. "It's like comparing silent films with cinema today," he says.

Like GPS, Tango requires specialized hardware and software. And both are best appreciated once experienced. As Lee puts it: "If you asked people in 2000 whether or not they needed a GPS in their pocket, most probably would have said no. But once people got GPS in their phones, and apps that made use of it, they were able to discover much more about their envi-

COURTESY OF THE MUSEUM OF NATURAL HISTORY; COURTESY OF WAYFAIR; COURTESY OF PROJECT TANGO

ronment than they could before. And now most of us wouldn't consider buying a phone without it."

To truly become an essential smartphone feature, however, Tango still needs to facilitate great apps. This is a work in progress. Jeff Meredith, who heads Lenovo's Android business group, says only about 50 "very good" Tango apps will be available in Google's online Play store when the Phab2 Pro goes on sale.

The hardware Tango requires will also need to be streamlined before it can become anywhere near as ubiquitous as GPS in phones. To support Tango, manufacturers must outfit phones with special equipment, including a depth sensor that uses infrared signals to measure distance to points in space and a fisheye-lens camera for wide-angle viewing and motion tracking. Those components increase a phone's girth, heft, and cost. (The Phab2 Pro is larger and heavier than Apple's biggest smartphone.) The extra gear also draws more battery power and generates additional heat that needs to be dissipated. In contrast, phones get GPS functionality from a tiny chip and antenna.

Then again, GPS gear once was much larger, but it shrank over the years as mass adoption drove technological advances. Lee is hoping Tango will follow the same trajectory. His team recently worked with the mobile-chip maker Qualcomm to get its popular Snapdragon processors to support Tango cameras, sensors, and algorithms. Providing phone makers with processors that combine multiple Tango functions in a single chip will save some space inside phones, reduce power consumption, and make the technology easier to deploy.

Ultimately, Tango will be most useful if it also gets baked into things other than phones, from robots to wearables, and if those devices all share data about areas they have mapped. Tango, for example, could allow robots to navigate around the furniture and rooms in your house. Lee envisions a future in which a person could tell a Tango-enabled robot, "Go to the door," and it would instantly know where to head.

If Tango improves the situational awareness of many of the devices we rely on, this add-on to today's smartphones will end up creating what Lee calls "a new class of computing."

Elizabeth Woyke is an editor for Business Reports at MIT Technology Review *and the author of* The Smartphone: Anatomy of an Industry.

The Light Fails to Glow on DIY Biology

Biohacking remains a revolution without a product.

By Antonio Regalado

In any discussion of biohacking, Exhibit A is likely to be the "glowing plant," the wildly successful 2013 Kickstarter campaign that raised $484,013 to create bioluminescent plants visible at night.

The project captured an idea with growing cachet: that DNA is just computer code, living things mere hardware. This view has been reinforced by the quickly falling cost of both reading the DNA molecule and synthesizing it. If biology can be managed from a computer screen, if it is de-skilled and democratized, then what follows is what the glowing-plant team calls "a world where bio-engineering is as easy and commonplace as mobile application development is today."

Just one problem, though. There is still no glowing plant. The project, which has since morphed into the company Taxa Biotechnologies, has not made any plants that emit light unassisted. The seeds it promised to its backers are already two years overdue. "What it says is that biotechnology is not as easy as portrayed in the popular media," says Todd Kuiken, a scholar at the Woodrow Wilson Center in Washington, D.C., who studies synthetic biology and was among the backers of the project. "All these stories that people are going to make viruses or new animals in their garage—well, it's just not as easy as connecting Legos together."

Do-it-yourself biology promises to let ordinary people or small teams of amateurs participate in what is already a great scientific revolution shaping the 21st century. Lately, the DIY biology movement has gravitated to "synthetic biology," the trend in academia and industry that advocates for precise and extensive engineering of living things, genetic modification using off-the-shelf DNA "parts," and even construction of complete life forms synthesized from raw materials.

The combination of DIY biology and synthetic biology—biohacking, in other words—is so far mostly rhetorical. Yet the Kickstarter campaign certainly made it sound easy. Its creators said they would take genes from fireflies or bioluminescent bacteria and add them to a plant to make it emit a greenish light. Anyone who donated $40 was promised a plant within 12 months. For a $150 contribution, you'd get a glowing rose. The project's core aim has been to add six genes to the genome of tobacco plants and coördinate them as an entire metabolic pathway.

But that has proved very difficult to do. "It was a poor choice of product. It's on the edge of what's possible," says Antony Evans, the Cambridge University math major, former mobile-app marketer, and entrepreneur who is CEO of Taxa and heads the project. "I personally feel terrible we haven't shipped yet. But it's not like we took the money and ran." Just the opposite: rather than conceding defeat, Evans this summer raised another $250,000 on Wefunder, a site that allows any member of the public to buy shares in risky private companies. It's like a new Kickstarter, this time with stock instead of products in return. Evans says the new funding will first go to a different, more feasible product—a fragrant moss with a single added gene that makes it smell like patchouli oil—but that the team is still working on the plant.

Glowing Plants: Natural Lighting with No Electricity
Created by Antony Evans
on Kickstarter.com

"Synthetic Biology and Biosecurity: Challenging the 'Myths'"
By Catherine Jefferson, Filippa Lentzos, and Claire Marris
Frontiers in Public Health
August 2014

Growing trend

The glowing-plant project is so far the highest-profile venture to come out of the do-it-yourself biology community. There are now some 86 DIY biology spaces or groups around the globe, in places including Auckland, Kansas City, and Paris, according to a tally kept by the website DIYBio.org. The grandfather of the DIY spaces is GenSpace, based in Brooklyn, a nonprofit membership group whose founder, the biologist Ellen Jorgensen, has emphasized the movement's educational purpose, saying that "the best way to understand biotechnology is to experience it through practice."

The DIY movement is mostly hobbyists and educators, but increasingly it also has the ambition to create medicines or new consumer products outside of big companies or academia. Projects under way include an effort to produce milk protein in modified yeast cells so it can be used for cheese making. Another team is attempting to make human insulin in bacteria, reinventing something first achieved by the biotechnology industry in 1978.

The significance of such independent undertakings was described by physicist Freeman Dyson in "Our Biotech Future," an influential 2007 essay in the *New York*

MATT PANUSKA

Review of Books. Dyson argued that the trend embodied by digital cameras, personal computers, and GPS receivers would "soon be extended from physical technology to biotechnology." He also anticipated how home-brew projects would derive their importance from their ethical thrust—insulin free of drug-company profits, cheese without dairy cows, light without electricity. Instead of Monsanto with its labs full of experts striving for the next pesticidal seed, a new "domestic" biotechnology would be oriented toward green technology with utopian aims.

The Kickstarter campaign for a glowing plant succeeded because it tapped into these aspirations. "It was the first big synthetic-biology project that had ever been crowdfunded," says Maria Chavez, director of community engagement with BioCurious, a DIY lab in Silicon Valley. Evans understood that his group was selling not just a plant but a vision that, much as 3-D printers had done, promised new sources of invention, creativity, production—and profits. If DNA was really just code, then biohacking could be seen as a modern version of the Homebrew Computer Club, the 1970s hobbyist group that spawned the first Apple computer and, eventually, the world's largest company.

What the team didn't budget for was how hard engineering the plants would

be. They knew a dimly glowing tobacco plant had been made before, in 2010, but the scientist who carried out that work, Alexander Krichevsky, says it took him three years leading a lab at a well-equipped university, SUNY Stony Brook, to do it. Krichevsky has since started his own glowing-plant company, Bioglow, and says he has spent another three years trying to make the plants bright enough to interest consumers, a task that is ongoing. He says it was obvious to anyone in plant biology that Taxa's time lines were unrealistic. "I was surprised by the promises they made. I thought, maybe they know something I don't. Now I see that it is delusional," he says. "They didn't deliver anything for three years, and I strongly doubt they ever will."

Tacit knowledge

Indeed, the "supposed trend" toward greater ease of access to biological engineering is exaggerated, says Claire Marris, a sociologist of science at City University London. That misperception, she says, has led to unfounded fears over home-brew garage bioterrorism, such as when the European Commission in 2007 warned of the possibility of "à la carte" viruses and microbes. In fact, Marris says, engineering actual products, like terror germs, is so difficult that such concerns are not realistic. She points out that biological work, rather than being scripted, is heavily influenced by "tacit knowledge," like the secrets of a chef that don't appear anywhere in a written recipe.

The glowing-plant team did manage to carry out many scientific steps without touching a petri dish. Gene sequences were designed on computers and fetched by mail order from distant supply houses. The strands were even fused into a longer genetic program using a rent-a-lab operated by other entrepreneurs. Yet while it was possible to script a bioluminescent program, instantiating it inside a plant is much harder. The organism doesn't want to waste its energy on an extraneous process like glowing, and it is liable to undertake complex countermeasures. Even if six genes are added correctly (itself a daunting challenge), the plant will furiously attempt to silence or extinguish them, says Krichevsky. That leads to a challenging scientific problem solved only through grinding trial and error.

As it proved difficult, Evans and the project's scientific founder, Kyle Taylor, a plant science PhD from Stanford, started clashing over the project's real purpose: was the glowing plant a potentially important new business or just a DIY demonstration? The conflict reflected the larger question facing DIY biology.

In 2014, the team made it into the first class of biotech companies to be accepted into Y Combinator, the high-profile tech accelerator that invests $120,000 in each startup and helps it polish an investor pitch—a process that has produced phenomena like Airbnb and Dropbox. Y Combinator's organizers believed that it had become easier for small groups of entrepreneurs to build potentially significant companies in biology, opening biotech to the rapid time lines and change-the-world investor pitches so common in software. The biotech graduates of the program include Ginkgo Bioworks, the Boston synthetic-biology company that recently raised $100 million from software investors.

Evans, the entrepreneur, was probably correct that a glowing plant, inexpensively propagated in a greenhouse and sold as novelty, could make people wealthy. Some entrepreneurs had previously engineered aquarium fish to fluoresce in red, yellow, or green under a fish tank's light, and the rumor was they had struck it rich. But the plant hackers couldn't get rich unless the plant glowed. And Evans says he almost gave up this February. That is when Taxa tested plants into which they'd inserted a genetic cassette they were sure would work. Instead, they found the plants didn't emit any light at all. They were duds. It appears one of the genes had broken when it was fired into the plant. "That was the first time I started to have doubts about whether we would ever get there," says Evans.

As for Taylor, he says he always saw the point as inspiring people to get interested in science, not raising more money. The Kickstarter campaign "was an interesting case where you could have a voyeuristic look over my shoulder, to show what goes on in a lab is pain, hard work, and failure," he says. "I viewed it as educational. But that isn't the way it was viewed by others." By the time of the campaign, he'd also concluded that getting a plant to glow in a way that is visible to the naked eye was going to be difficult. "As I dug in more, the depth of the problem became much more apparent. I started to understand what it would take to become an actual product," he says. He resigned from the project in 2015 and now says, "I am trying to put the glowing plant behind me."

For now, there are still lots of true believers in Taxa and synthetic biology, and by many accounts the project succeeded as an educational venture. Evans has posted more than 60 updates, offering blow-by-blow details of the team's efforts and struggles. Josh Melnick, a student from Ohio with a master's in microelectronic engineering, wrote to tell me he has "been taken for $250" by the project. Yet he says it inspired him to start studying genetic engineering, and he's begun hanging around DIY biology labs. "I have fallen under the allure of synthetic biology," says Melnick, who dreams of making a new living thing all his own. Whatever he makes, he expects that it will probably be more of an art project than a product.

Antonio Regalado is senior editor covering biomedicine at MIT Technology Review.

Demo

Zhenan Bao

Electronic Skin

In Zhenan Bao's lab at Stanford, researchers are inventing materials for touch-sensitive prosthetics.

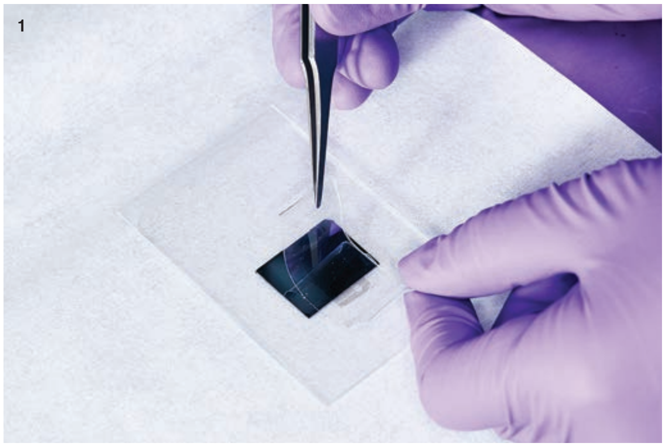
By Katherine Bourzac
Photographs by RC Rivera

The human hand has 17,000 touch sensors that help us pick things up and connect us to the physical world. A prosthetic hand or foot has no feeling at all.

Zhenan Bao hopes to change that by wrapping prosthetics with electronic skin that can sense pressure, heal when cut, and process sensory data. It's a critical step toward prosthetics that one day could be wired to the nervous system to deliver a sense of touch. Even before that is possible, soft yet grippy electronic skin would let amputees and burn victims do more everyday tasks like picking up delicate objects—and possibly help alleviate phantom-limb pain.

To mimic and in some ways surpass the capabilities of the skin on human hands, Bao is rethinking what an electronic material can be. Electronic skin should be not

1



1 A researcher makes a transistor on a stretchy rubber material that acts like a sticker. As the rubber is peeled from the glass, it picks up a layer of semiconducting carbon nanotubes that will form the active area of the electronic switch.

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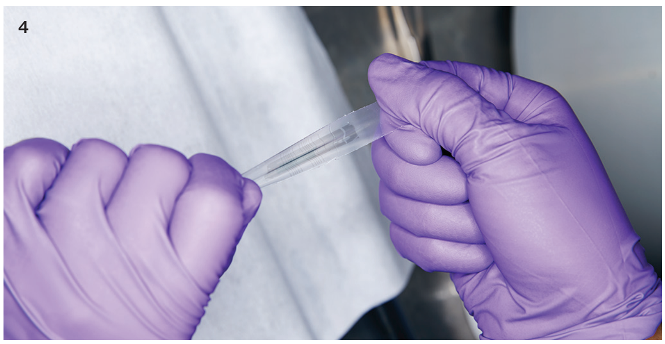
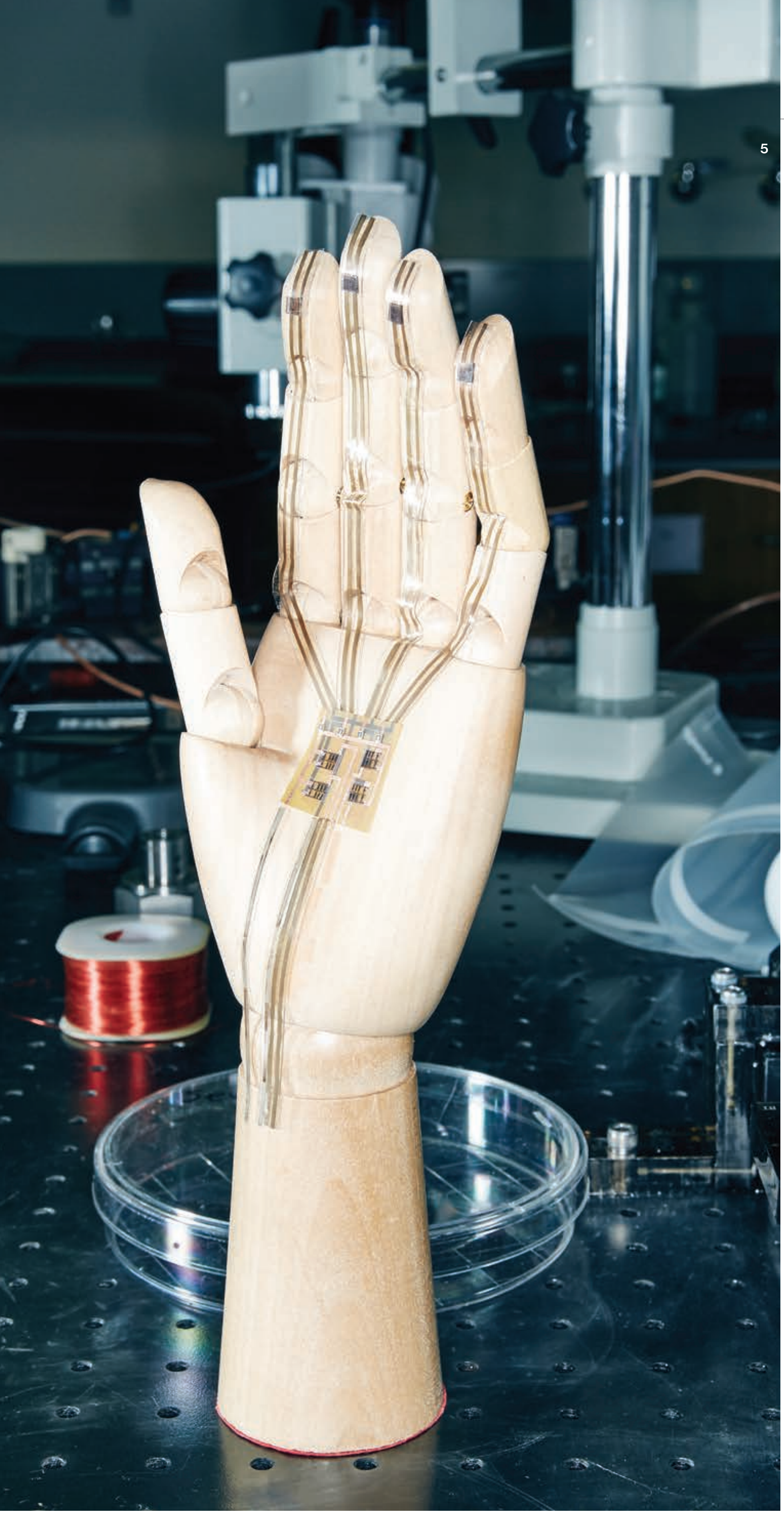


2-3 A slide is coated with an insulating material that will help turn the stretchy transistor off. Inside this machine, a small platform will spin the slide to make a thin, smooth film.

4 This stretchy transistor is made of carbon nanotubes, electronic polymers, and silver-nanoparticle ink. It could be used in circuits that process data from touch sensors.

5

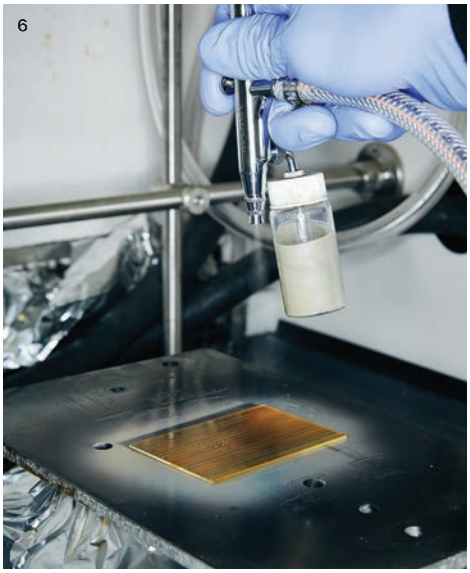


5 Each fingertip on this wooden display hand is fitted with a stretchy touch sensor connected to electrical leads that carry data to a flexible electronic control center on the palm.

6 An airbrush loaded with silver-nanoparticle ink can be used to print electrical contacts and wires through a stencil.

7 Through a microscope, tiny pyramids on a touch sensor are visible. These 50-micrometer-wide features improve sensitivity, just like the ridges of our fingerprints.

6



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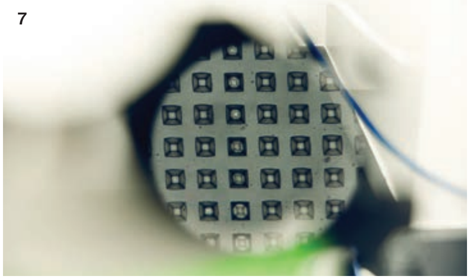
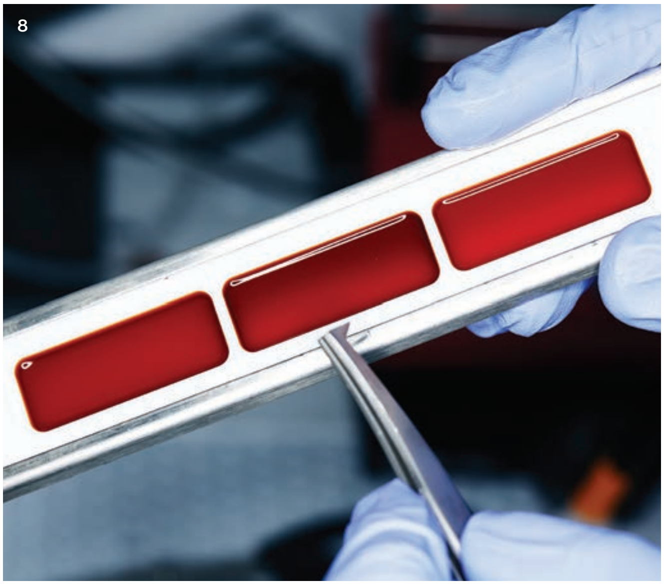
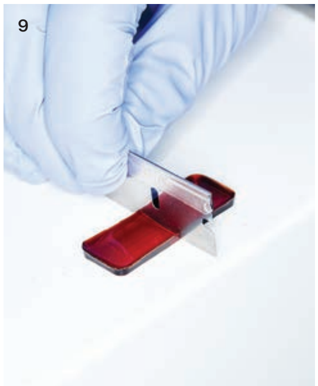
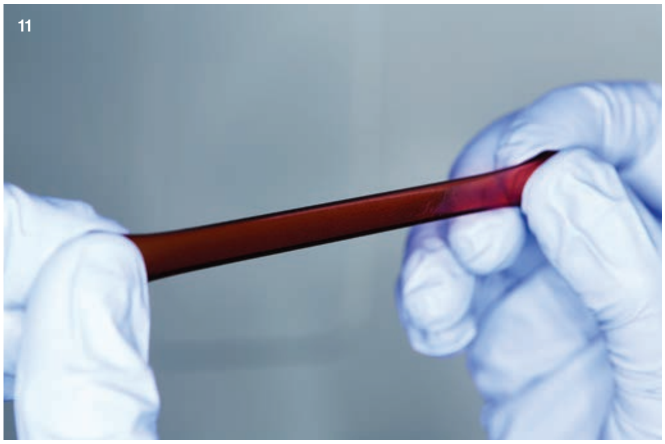








8 This material mimics two important features of human skin: the ability to stretch and wrinkle, and to heal.

9 A researcher cuts the rubbery material in two.

10 Less than a minute after the cut pieces are put back together, they've rejoined.

11 The healed material can be stretched much more than human skin can be without breaking.

only sensitive to pressure but also lightweight, durable, stretchy, pliable, and self-healing, just like real skin. It should also be relatively inexpensive to manufacture in large sheets for wrapping around prosthetics. Traditional electronic materials are none of these things.

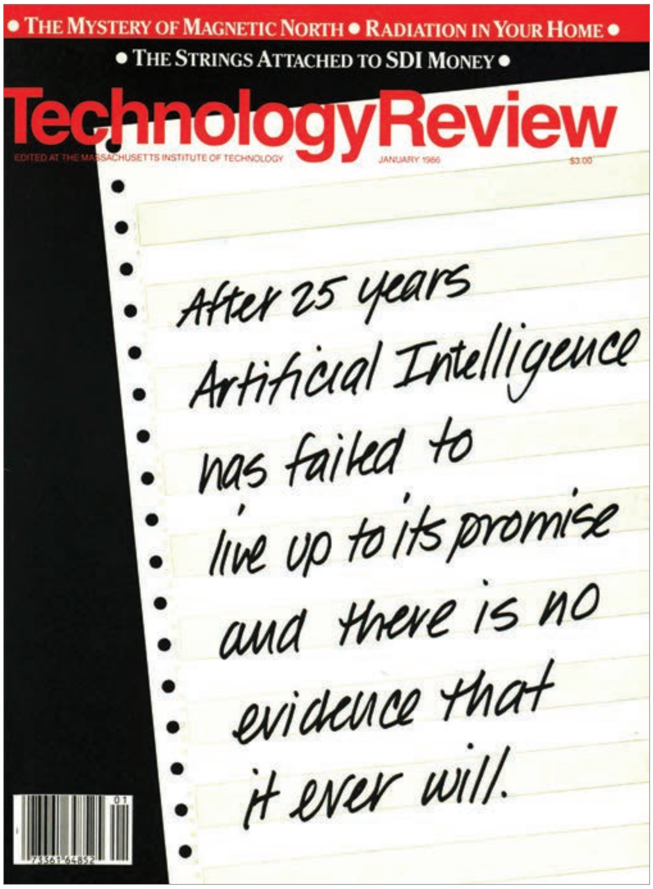
Bao (an *MIT Technology Review* Innovator Under 35 in 2003) has been working on electronic skin since 2010. She has had to create new chemical recipes for every electronic component, replacing rigid materials like silicon with flexible organic molecules, polymers, and nanomaterials.

Bao's group uses stretchy rubber materials that are similar to human skin in the way they give and recover. Sometimes her team mixes electronic materials into the rubber; other times they build on top of it. To make a touch sensor, researchers mix in carbon that is electrically conductive. The voltage across this conductive rubber sheet changes when the material is pressed. Bao's group found that covering these touch sensors with a pattern of microscale pyramids improves their touch sensitivity—much as the whorls of our fingerprints do. Depending on the design, these sensors can be made at least as sensitive as the skin on our hands. Her group also prints transistors, electrical leads, and other components on the rubbery skins to make stretchy circuits that could process data from touch sensors on a prosthetic hand.

Now Bao is working on weirder materials. One polymer she developed is much stretchier than human skin: it can be pulled to 100 times its normal length without breaking. This material also heals when cut, without any heat or other trigger. And it can act as a weak artificial muscle, expanding and contracting when an electric field is applied.

With the basic materials and designs in place, she's working on semiconductors and other electronic materials that have the same healing and stretching prowess. But reinventing the electronic materials won't be enough: data from these artificial skins has to be delivered to the nervous system in a format that the body can understand. Bao's group is now working on circuit designs that will send signals to the nervous system, so that electronic skins will one day not only help amputees regain dexterity but also let them feel the touch of their loved ones.

30 Years Ago



Communication Breakdown

A pair of experts mulled whether we'd ever get machines to talk, let alone think.

"Computers will not be first-rate teachers unless researchers can solve four basic problems: how to get machines to talk, to listen, to know, and to coach. 'We speak as part of our humanness, instinctively, on the basis of past experience,' wrote Patrick Suppes of Stanford University, one of the pioneers in computer-aided instruction, in a 1966 *Scientific American* article. 'But to get a computer to talk appropriately, we need an explicit theory of talking.'

Unfortunately, there is no such theory, and if our analysis of human intelligence is correct, there never will be. The same holds true for the problem of getting computers to listen. Continuous speech recognition seems to be a skill that resists decomposition into features and rules. What we hear does not always correspond to the features of the sound stream. Depending on the context and our expectations, we hear a stream of sound as 'I scream,' or 'ice cream.' We assign the space or pause in one of two places, although there is no pause in the sound stream. One expert came up with a sentence that illustrates the different ways we can hear the same stream of sound: 'It isn't easy to wreck a nice beach.' (Try reading that sentence out loud.)

At this point the reader may reasonably ask: If computers used as logic machines cannot attain the skill level of expert human beings, then why doesn't the public know that? The answer is that AI researchers have a great deal at stake in making it appear that their science and its engineering offspring are on solid ground. They will do whatever is required to preserve this image."

Excerpted from "Why Computers May Never Think like People," by Hubert and Stuart Dreyfus, brothers and coauthors of the book Mind Over Machine, *in the January 1986 issue of* Technology Review.

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